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ELECTROENCEPHALOGRAPHY IN RELATION TO OTOLOGY.*†‡

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In the last five years the measurement of the electrical currents produced by the human brain has been used as a diagnostic aid in many large hospitals. The electroencephalogram, or brain wave as these tracings are called, was first developed in the experimental laboratory of Prof. Hans Berger, of Jena, Germany, in 1929. Like the electrocardiogram of Prof. Einthoven, described in 1907, it was regarded at first by physicians as a curiosity of little clinical value and a suspicious, complicated gadget by the skeptics. Since 1935, when Gibbs first used this machine for the study of brain electrical discharges in epileptics at the Boston City Hospital, its clinical use has spread to most of the large neurological centers in this country.

An article by the author, "The Clinical Application of Electroencephalography,"[1] fully describes the laboratory setup, techniques and apparatus. The new and excellent Atlas by Gibbs and Gibbs[2] is highly recommended to anyone wishing to look over a large variety of clearly reproduced electroencephalographic tracings.

Papers by Davis[3] and Jasper[4] deal with the general problems in normal and abnormal tracings, and Denis Williams

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has the best papers on head injuries and localization of tumors.[5,6] The bibliography of this subject, in spite of its recent origin, is extensive and the reader is referred to the complete bibliography in Gibbs' Atlas[2] for further articles.

With modern apparatus the procedure of obtaining tracings of human brain potentials is a relatively simple task. The subject is made comfortable in a chair or on a bed in a quiet room. For ordinary recording to see if the waves are normal

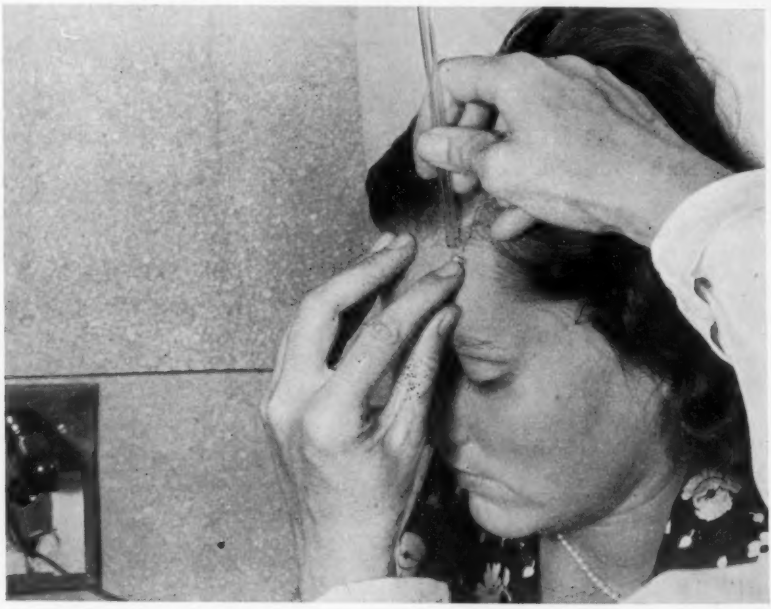

Fig. 1. Placing an electrode on the left frontal region. The little solder disc is under the index finger of the technician. Air from the glass tube dries the collodion which covers the electrode.

or abnormal, four to six electrodes must be fastened to the scalp. Usually two or three are placed on each side of the head. The hair is not cut. The scalp is lightly cleaned with a little acetone over points 2 cm. in diameter on frontal, parietal and occipital regions. Onto these clean surfaces a bit of ordinary electrocardiographic electrode paste is well rubbed. A 5 mm. or 10 mm. flat solder disc fused onto the bared end of a No. 32 enamel wire forms the electrode (see Fig. 1).

The solder disc is placed firmly on the electrode paste area and then covered with collodion, which is dried by a compressed air jet (see Fig. 1), or hair drier, or even the air from a rubber bulb. The dried collodion holds the electrode firmly to the scalp and, if one is careful, a good electrical contact is made. The other end of this wire is fastened to some form of a pin jack for insertion into the panel board, connected by means of a shielded multi-wire cable to the recording apparatus. There should be about 5 to 20,000 ohms resistance as measured with a pocket tester between any two electrodes on the scalp. When the electrodes are in place, the

Fig. 2. Close-up of a standard three pen Grass writer in operation. Note the normal 10 per second alpha rhythm being recorded. There is both a signal and timing pen in operation.

pin ends are plugged into the board at the patient's head. The subject is told to close his eyes, relax his facial, jaw and neck muscles and be as quiet as he can.

The recording and amplifying apparatus which are and look like special radio sets are especially built for this purpose by four engineers in this country. They are Lovett Garceau, Holliston, Mass.; Albert Grass, Harvard Medical School, Boston; Franklin Offner, Chicago; and Rahm Instruments Inc., 12 West Broadway, New York. These amplifiers receive the tiny pulsating electric waves picked up from the scalp electrodes and amplify them about a million times in strength so that they are strong enough to move a pen, which is then

able to reproduce the waves on rolled paper in the manner of a ticker tape machine. The electric discharges from the brain then appear as wavy ink lines directly on the paper (see Fig. 2). Usually most laboratories have enough equipment so two to six parts of the brain can be examined at once and thus the recording paper has two to six separate lines on it. These multiple channel machines are particularly necessary in the localization of intracranial lesions (see Fig. 3). The

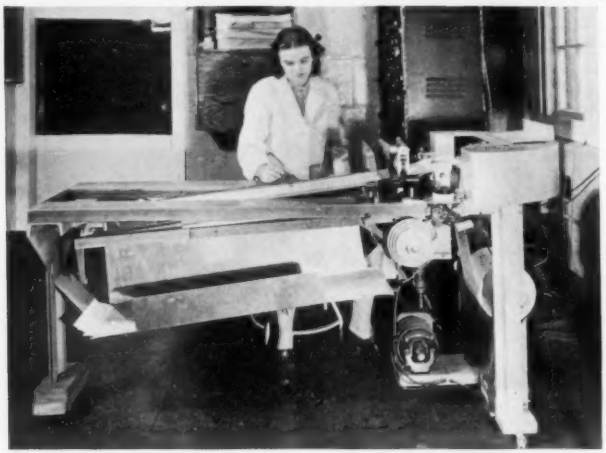

Fig. 3. A six pen special ink writing oscillograph designed and built by Dr. Alfred Loomis, of Tuxedo Park, and presented to the Brain Wave Laboratory for clinical use. The banks of amplifiers are in the background.

speed of the recording paper is constant 3 cm. per second and usually a timing pen marks off each second, so the number of waves per second is readily measured. It is well to realize here that the voltages of the actual brain wave is 1/20 of the electrocradiogram, hence the complicated apparatus required to register it. The usual electrocardiogram voltage is 1/1,000 of a volt (1 millivolt), whereas the electroencephalogram voltage is 1/20,000 of a volt (50 microvolts).

The normal electroencephalogram for adult humans differs slightly from one person to another, but there are two general characteristics that are found in all healthy people.

1. There are two types of normal brain rhythms and all individuals with normal central nervous systems show vari-

ous percentages of these two groups. The first or *alpha* waves have an eight to 12 per second frequency with smooth, regular and clear-cut patterns, with voltages from 30 to 125 microvolts. These waves temporarily disappear when the eyes are opened or if one has a problem to work out, such as a calculation. The second or *beta* group of normal waves consists of faster frequencies — 19 to 30 per second, more irregular, and of lower voltages — 10 to 30 microvolts. They are unaffected by attention or effort.

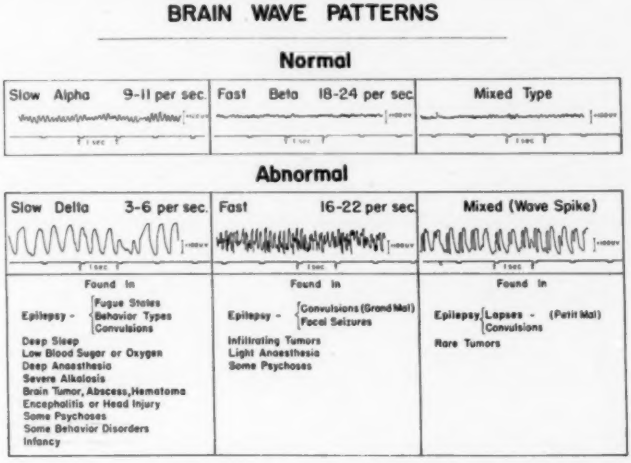

Fig. 4. The normal (top) and abnormal (bottom) brain wave patterns compared.

2. These normal waves are found all over the brain accessible to the surface electrodes on the scalp, the alpha typ being more prominent in the occipital region. Examples of such normal waves are shown in Fig. 4 (top).

In the brain with neurological disease, particularly where the pathology is near the surface, as in the cortex or white matter under it, very definite electrical disturbances in the brain wave pattern are encountered. The waves usually are greatly slowed in frequency, two to five cycles per second, and the voltages are increased from 75 to 300 microvolts. Less frequently there are abnormal waves of increased voltage in intermediate frequencies, 14 to 18 cycle or 28 to 34 cycle.

These may be associated with epileptic motor discharges and a variety of other nonmotor disorders. Combinations of abnormal slow and fast waves are seen, too, in petit mal seizures (see Fig. 4, bottom).

The abnormal electrical activity in the human is distributed into three categories: *1.* Paroxysmal bursts of abnormal waves lasting seconds to minutes and appearing in a record otherwise nearly normal. This represents the sort of findings we see in epilepsy and the pathological patterns coincide with

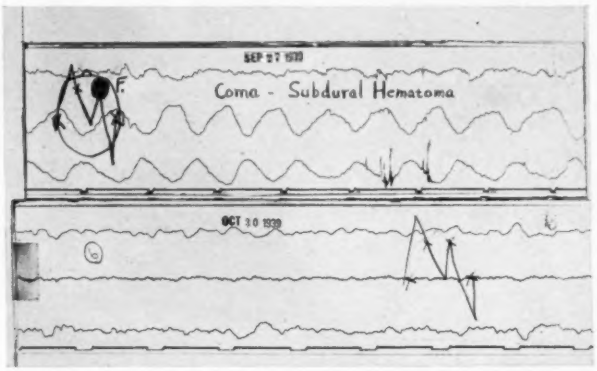

Fig. 5. Slow delta waves in a case of subdural hematoma showing the mirror-like phase reversal by which localization is determined. The bottom tracing shows relative normal pattern four weeks after successful removal of the correctly localized clot.

the clinical or subclinical seizures. *2.* Generalized, continuous, abnormal waves found all over the brain at all times. These are found in generalized cerebral diseases, such as trauma, encephalitis, etc. *3.* Localized, continuous, abnormal waves. These are found near focal scars, tumors, clots and abscesses (see Fig. 5).

In the Massachusetts General Hospital, the Brain Wave Laboratory since 1937 has functioned as a routine diagnostic service available to all divisions of the institution. About 2,200 examinations are done per year. One-half of these are for the purpose of aiding in the diagnosis of epilepsy in patients suspected of this condition. A quarter are research studies in normals or others, and a quarter are for the pur-

pose of establishing a *focal* electrical focus to aid in the localization of some discrete intracranial lesion, such as abscess, tumor or clot.

Before discussing the specific subject of brain abscess and the brain wave findings, the results of intracranial localization in general will be discussed. A group of 503 such localizations in the year 1939-1940 were carefully followed up to see how accurate the results were. This part of the investigation was done with the help of Mrs. Margaret Thompson. There were three sorts of brain wave reports:

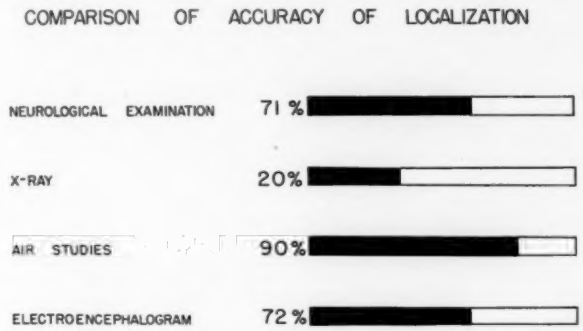

Fig. 6.

A. Positive localization, where a fairly clear electrical focus could be seen and demonstrated.

B. Doubtful localization, where the abnormal electrical discharges were diffuse and only a guess as to which area was more involved could be made.

C. Negative localization, where a normal record was found.

In the A group the correct localization (verified at postmortem or operation) was 85 per cent; in the B group it was only 55 per cent; combined, it was 72 per cent. In the C group, clinical follow-up showed 91 per cent agreement. Comparing these results with a neurological, X-ray and air studies, we see that electroencephalography is a very useful localizing tool (see Figs. 6 and 7).

Applying the electroencephalogram specifically to the problem of brain abscesses, we have the following data to present:

Fifteen cases of proven cerebral abscess were examined by means of electroencephalography. In seven an electrical focus was found correctly localizing the abscess. In seven others the brain waves were diffusely abnormal. In only one was a negative examination encountered, and in that the abscess was in the cerebellum. The data is summarized in Table I. An example of a case follows:

A 33-year-old white, married clerk with chronic bronchiectasis for 18 years, five days prior to admission had twitching and numbness of the right hand, and three days prior to admission right Jacksonian fits of the face and arm. Neurological examination showed the left disc hazy, right arm paretic, a question of hemihypesthesia of the arm, the right abdominal reflex absent, and some alexia. Lumbar puncture showed a pressure of 50 and a total protein of 43. Electroencephalogram localized the lesion in the left parietal temporal region. An exploratory operation showed an abscess in the left parietal temporal region.

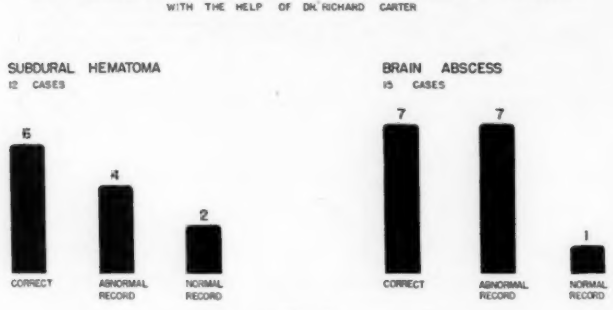

Fig. 7.

From this small series of cases it is seen that, first of all, the electroencephalogram was *abnormal* in 14 of 15 cases, and second, the presence of a sharp electrical focus *when encountered* was correct in its localization. This would suggest that the use of electroencephalography in suspected cases of brain abscess was a valuable aid in localization, and a negative electroencephalogram is strong evidence against an abscess.

A group of verified subdural hematoma patients who had electroencephalograms furnishes interesting data to compare with the brain abscess group. Here, in 12 cases, 10 had abnormal records and six had correct electroencephalographic

localization. The two groups are compared in Fig. 7. Again, it is to be noted that a negative electroencephalogram is strong evidence against a subdural hematoma.

It is well at this point to emphasize that this procedure is only a laboratory test, subject to the errors and misinterpretations of any complicated laboratory investigation. An analy-

TABLE I.

Case No.	Unit No.	Initial	Age	Source	N.E.	X-ray	Type of Abscess	Electro-encephalogram	
1	244638	O.F.	34	S	/	X	Rt. Cerebellar	C	X
2	246840	F.S.	24	S	/	O	Rt. F. Subdur.	B	O
3	158608	S.L.	19	S	/	—	Lt. Fron. Par.	A	/
4	91368	B.R.	18	E	O	O	Lt. Fron.	A	/
5	47606	A.L.	13	E	/	O	Lt. Ex. D. Temp.*	B	O
6	205800	R.V.	24	S	O	/	Lt. Fron.	B	X
7	214053	J.C.	29	L	O	O	Rt. Par.	A	/
8	251539	J.C.	9	S	/	/	Rt. Fron.	B	X
9	256008	S.C.	9	E	O	/	Lt. Temp.	A	/
10	258452	T.D.	32	L	O	O	Lt. Fr. Temp. Par.	A	/
11	309799	D.H.	32	E	O	O	Lt. Temp. c Meng.	B	O
12	223602	R.S.	13	S	/	O	Lt. Subdur.	B	O
13	306974	C.B.	60	E	/	O	Lt. Temp. c Meng.	B	/
14	270071	B.G.	30	S	O	/	Lt. Subdur.	A	/
15	179578	M.F.	20	E	O	O	Lt. Temp.	A	/

A — Positive localization
B — Doubtful localization
C — Negative localization
/ — Correct
X — Wrong
O — no conclusion
S — Sinus
E — Ear
L — Lung
* — Left extradural temporal

TABLE II. SOURCES OF DIFFICULTIES IN 90 CASES.

Deep or posterior fossa lesion	39
Patient very unco-operative	15
Too few electrodes	10
Artifacts	5
Error in interpretation	2
Unexplained	20

sis of such difficulties in 90 cases is summarized in Table II. It is obvious that the deep or posterior fossa lesions are the hardest to localize by means of the electroencephalogram. On the other hand, such deep-seated processes usually are easy to localize by ventriculography and cause neurological signs that aid in the diagnosis.

It is essential, therefore, to utilize all of the existing sources of localization if we are to be truly accurate and not allow a new procedure to displace well tried older ones. Where electroencephalographic and air studies agree, *no* errors in our

series have been encountered. Where electroencephalographic and neurological findings agree, 95 per cent correct results are found.

A further point worth considering is the fact that this procedure does not hurt, upset, or risk the patient's life in any way. If a satisfactory record for any reason is not obtained, a repeat test can be run the next day.

A few words might well be added here on the interpretation and running of the apparatus. These machines are very delicate and highly sensitive. They require trained personnel to operate them and care and thought in keeping them in efficient, reliable working order. At the present time it seems wiser to set them up in a large general hospital, where adequate space and repair and maintenance facilities are available. Furthermore, they are expensive, a reliable set costing around $1,500, and $500 to install and keep up the first year. Portable or office outfits, although available, do not seem practical for accurate localization work at the present time. It is wiser to send the patient to the laboratory for the test, and in most large cities such laboratories are now available.

Interpretation, although not complicated, requires experience and certain training, both of which can be obtained in six months working in one of the established laboratories. With this conservative approach, this new field of diagnosis will not lead us astray or discredit the pioneers who developed it.

Further uses of the electroencephalogram to the otologist: *1*. The brain wave changes in the normal alpha rhythm from hearing a sound might be of some help in working out the diagnosis of malingered deafness from true deafness. We are not impressed with the reliability of this because many deaf people hear some notes — particularly loud overtones — and would, therefore, show the characteristic disappearance of the alpha waves. *2*. The recording of nystagmus is simple to do, but it is not clear what use clinically the nystagmogram could be. *3*. In Ménière's disease on the affected side some fast, high voltage, abnormal activity in the electroencephalogram has been seen in five or six cases, which disappears when the vertigo leaves. This has not been a constant enough finding to be recommended for diagnostic purposes. *4*. In a

study of chronic seasickness with the electroencephalogram, by the same author at a Naval Hospital, a greater number of susceptible individuals were found with high percentages of alpha waves than other normal patterns. This is only of academic interest at this time but does tie up with similar findings in gastric ulcer patients.

SUMMARY.

1. The electroencephalogram in normal and abnormal brains is briefly described.

2. The results of 500 localizations in intracranial lesions in general is discussed.

3. The results of 15 localizations in cerebral abscesses are reported and the fact that 14 such cases had abnormal records suggests that a negative brain wave is good evidence against abscess.

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ENCEPHALOGRAPHY IN OTOGENIC AND RHINOGENIC COMPLICATIONS.*†

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Injection of air into the ventricles of the brain was at first undertaken for the differential diagnosis of the different forms of hydrocephalus and for the diagnosis of brain tumors.[1,2] Inflammatory diseases of the brain and meninges were considered as demonstrable by encephalography at a much later time, so that the interest of otolaryngologists in this procedure dates only since the past decade.

The main purpose in presenting the following observations is to awaken greater interest in encephalography on the part of the otolaryngologists.

It may not be amiss to point out that air can be injected into the ventricles of the brain not only directly through the skull or the atlanto-occipital membrane but also by lumbar puncture. I have most often made use of the latter method, occasionally occipital puncture, and never by direct approach to the ventricles. This discussion is, therefore, restricted to the two first-named procedures.

TECHNIQUE.

The technique we have employed for lumbar encephalography is essentially the one now in vogue. Patients are given three grains of sodium amytal the preceding evening. This same dose is repeated the morning of the examination, without breakfast. Fifteen minutes before the operation, one-sixth or one-quarter grain of morphine is given hypodermically. This routine is altered in small children, who are given one-twelfth grain of morphine hypodermically one hour before, and one-half of one grain of sodium amytal one-half hour prior to starting the puncture.

As a precautionary measure against cardiac collapse, some physicians administer one-half of a tablet of ephetonine

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(0.025 gm.) 30 minutes before undertaking the injection of air. General anesthesia is contraindicated because it not only prevents the entry of air into the ventricles but also enhances the risks involved. Morphine, too, has been rejected, notably by Bohn,[3] who observed that patients frequently not only show a pronounced depression of the vital centers which necessitate stimulation during the procedure, but are often demoralized so that the injection has to be interrupted until it can be finally carried out under proper sedation. He advises substituting atropine sulfate (1/100 to 1/25 gr.) for the opiate.

It is highly desirable to begin the operation in the X-ray room, but where the needed facilities are lacking one must of course be content with taking the patient to the X-ray room after the air has been injected.

The procedure proper is comparatively simple: Spinal puncture is carried out and the pressure of the spinal fluid determined by the manometer while the patient is in a horizontal position. The patient is then directed to sit up slowly, with the head moderately flexed on the trunk, which position is essential for the air to enter the ventricles. With needle *in situ*, it is of utmost importance and cannot be stressed too emphatically that the fluid should be withdrawn slowly and a lesser quantity of air slowly introduced. I prefer removing only 5 cc. of fluid at first and then injecting 3 cc. of air. Then I again slowly withdraw 10 cc. of fluid and likewise again inject 6 to 8 cc. of air. There are some who claim that it is possible to improve the visualization of the ventricles by quickly injecting 5 or even 10 cc. of air without first withdrawing fluid. I have never tried this procedure.

It may occasionally happen that the flow of the fluid stops before the desired quantity has been removed. In such cases the needle should be slightly changed in position or the head bent slightly backward. Should signs of cardiac collapse appear, the patient must be placed in the horizontal position without disturbing the needle, and stimulants should be administered. Aromatic spirits of ammonia, caffeine sodium benzoate, hypertonic dextrose, adrenalin, pituitrin, digifolin or brandy may be used as seems indicated. The same measures are carried out when there is a complaint of nausea. It goes without saying that in the presence of respiratory

embarrassment the needle must be withdrawn and the inhalation of oxygen started without delay.

Once air has been introduced, X-ray exposure must be made at once. The otolaryngologist should ask the radiologist to

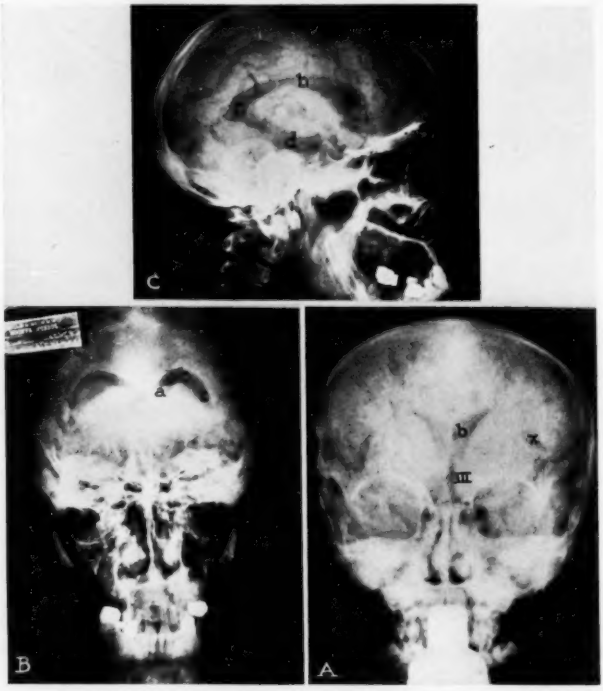

Fig. 1. Normal encephalograms. (A) presents an antero-posterior view; (b) indicates the anterior horn and the cella media; (III) the third ventricle; and (x) the enlarged cisterna fossae Sylvii on the left side. Note the filling of the sulci of the convexity of brain. In (B), which presents a postero-anterior view, (a) indicates the cella media, (b) the junction between cella media and posterior horn, and (c) the posterior horn. In (C), which presents a lateral view, (a) indicates the anterior horn, (b) the cella media, (c) the posterior horn, and (d) the inferior horn. Note the enlarged sulci on the mesial surface of the brain.

focus the rays anteroposteriorly, posteroanteriorly and laterally (stereoscopic), as films so taken are of greatest value for the study of otogenic and rhinogenic complications. It is also desirable to carry out further X-ray studies after 24 hours.

Although for obvious reasons it is only under exceptional circumstances that one can obtain encephalograms of normal individuals, Fig. 1 presents almost normal findings in different X-ray exposures. Fig 1A is an anteroposterior view of the ventricles of a boy, 4 years old, who was unable to speak, although there was no deafness, and both labyrinths were excitable. The films were taken in general anesthesia, 90 cc. of air were injected and 95 cc. of spinal fluid were withdrawn. The dilatation of the cisterna fossae Sylvii on the left side is interesting considering the boy's speech defect.

Figs. 1B and 1C are a posterior-anterior and a lateral view of the ventricles of a man, 43 years old, who suffered from Ménière's syndrome. Twenty-five cc. of air were injected and 35 cc. of spinal fluid were withdrawn.

It should be stated that among clinicians there is no accord with regard to the quantity of air to be injected and the ratio to the amount of fluid withdrawn. It is noteworthy that the amount of air injected has ranged between 15 and 1,500 cc. In 22 lumbar injections, the records of which are in my possession, I have injected a minimum of 12 cc. and a maximum of 140 cc. of air, the mean being 40 cc. This quantity proved adequate for filling the ventricles and subarachnoidal spaces except in five instances when the filling proved incomplete or entirely absent. In four of these patients there was clinical evidence of closure of the foramina of Magendi and Luschka, as evidenced by the fact that two had cerebellar abscesses, one a progressive purulent encephalitis and one a chronic osteomyelitis of the occipital bone. The fifth patient had a carcinoma of the nasopharynx. In the latter instance the ventricles were incompletely filled, although 46 cc. of fluid were withdrawn and 41 cc. of air introduced.

So far as concerns the ratio of injected air to the fluid withdrawn, I have always injected a lesser amount except in three instances when more air was injected than the amount of fluid withdrawn, without any ill effects. Klein[4] obtained the best results from a ratio of 10 (air) to 11.2 (fluid); however, we did not adhere to any fixed amount because one is best guided by individual tolerance and variations. In our series there was frequently a difference of 10 cc. between the air introduced and the fluid withdrawn.

DISADVANTAGES.

The injection of air into the ventricles is by no means without danger. So far as ventriculography is concerned, Grant[5] finds a mortality rate of 6.2 to 8.2 per cent; Riggs,[6] 8.1 per cent; and Heidrich,[7] 12.3 per cent. Among 895 cases of lumbar encephalography, Heidrich found a mortality rate of 0.7 per cent, and Grant a mortality rate of 0.3 per cent. Up to now we are fortunate in having experienced no fatality.

It should not be overlooked that there are certain factors which render lumbar encephalography a rather hazardous procedure. Some patients complain of disagreeable reactions such as headache, emesis, chilliness, diaphoresis, restlessness, pallor, backache and circulatory irregularity. To these should be added paresthesias, mental confusion and pains in the thorax and the abdomen. These symptoms or part of those mentioned may last as long as six days, especially in cases of brain tumors. Bohn found that with a mean of about 68 cc. of injected air the undesirable reactions on the average lasted about two and one-half days. These and similar experiences clearly show the necessity of not carrying out the procedure to the limit of tolerance. Accordingly, every surgeon should exercise judgment in remaining below the point of tolerance rather than risk the development of profound disturbances in the human economy.

It should also be borne in mind that after encephalography one may occasionally note a rise of temperature up to 100.4° F., a leucocytosis up to 21,000, with a prevalence of polymorphonuclear cells, an increase of globulins in the spinal fluid and a stasis observed in the eyegrounds. These after-effects usually disappear within four days unless they are caused by the intracranial complication itself and not by the encephalography *per se*.

INDICATIONS AND CONTRAINDICATIONS.

In the presence of intracranial complications one should carefully weigh the indications and contraindications. In reviewing that problem, the most important axiom gained by experience is to exhaust all clinical and laboratory diagnostic measures before resorting to encephalography, and

even then only when there is no decided contraindication to be discussed. Our available diagnostic methods other than visualization of the ventricles, at least in otorhinologic practice, are such that the instances for the more drastic measure will be few and far between. Thus, in my own practice during the past decade the accumulated material is comparatively small, although even eight years ago I[8] stressed the value of encephalography in properly selected cases.

The contraindications to air insufflation may be summed up as follows: *1.* Comatose states. *2.* Pronounced disease of the heart and/or the aorta. *3.* Senility and its counterpart, extreme childhood. *4.* Acute respiratory infections, open tuberculosis or furunculosis. *5.* Increased intracranial pressure characterized by a choked disk over 2 diopters or lumbar pressure beyond 300 mm. of water in the sitting, and 200 mm. in the lying position. The reason for this contraindication is to be sought in the fact that the medulla may be forced into the foramen magnum if the increased cerebral pressure is not counterbalanced by the pressure in the spinal canal. It is clear that in such circumstances it would be wise to resort to ventriculography rather than lumbar puncture. This contraindication should be modified to the effect that in choked disk of 2 diopters or less, lumbar encephalography does not entail special risk. *6.* Suspected complications in the posterior fossa even in the absence of signs of increased brain pressure. If in such a case visualization of the ventricles is absolutely required, then the method of choice should be ventriculography.

In spite of this dictum, I carried out lumbar encephalography in two patients with an indefinite diagnosis of cerebellar abscess. In one the subarachnoidal spaces were filled but no air entered the ventricles, although 40 cc. of air were injected. Autopsy revealed a well encapsulated cerebellar abscess, edema of the brain and obstructive hydrocephalus; however, there was no diffuse meningitis. In the other patient I obtained a satisfactory filling of the subarachnoidal spaces, but the ventricles were only partly filled. This patient recovered after drainage of the cerebellar abscess.

It would, of course, be very good for the prognosis if we could make encephalograms in cerebellar abscesses because if the cerebellar abscess is combined with a communicating hydrocephalus that means the foramen Magendi is open.

Then we can conclude that the pressure in the posterior fossa is not very marked in such instances, then the surrounding encephalitis around the abscess is not very marked, and when the encephalitis around the abscess is not very marked, the prognosis is better; therefore, it should be worth while to do a lumbar encephalography but unfortunately the risk is too great, and therefore, up to now we have abandoned this method in cerebral abscess.

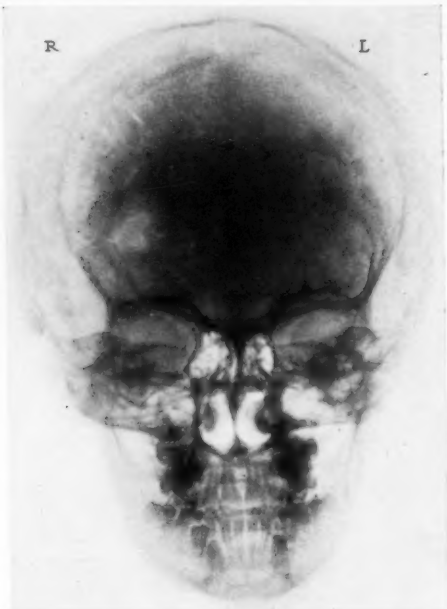

Fig. 2. Isolated filling of the right posterior horn in a case of cerebellar abscess on the right side. Anteroposterior view.

Figs. 2 and 3 present an anterior-posterior and a lateral view of the ventricles in that patient after withdrawal of 18 cc. of spinal fluid and injection of 14 cc. of air.

The fact that in that case the air entered the ventricles after injection of air into the lumbar canal proves that the foramina of Magendi and Luschka were not obliterated, as these foramina are the only openings through which the air can enter the ventricles from the lumbar canal. Contrary to this finding, the pathology indicates that in the majority of

cerebellar abscesses these foramina are obliterated due to the inflammatory edema of the cerebellum accompanying the abscess. In such cases obviously the air cannot enter the ventricles as actually occurred in the other cases of cerebellar abscess. Thus, lumbar encephalography answers precisely the question whether or not a cerebellar abscess is accompanied by a marked inflammatory edema of the cerebellum, the latter being the more favorable finding as far as the prognosis is

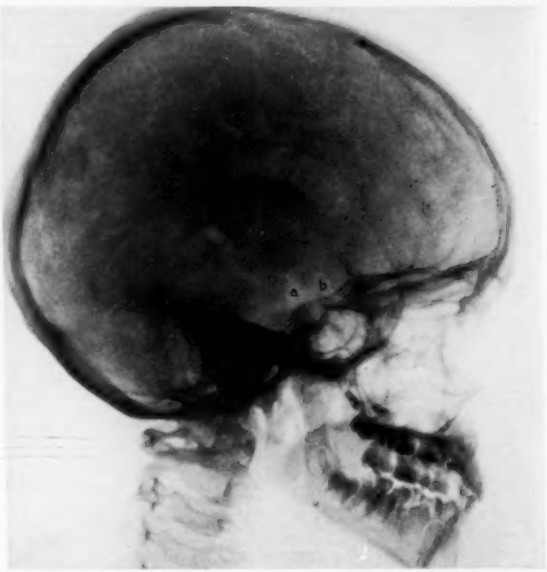

Fig. 3. Incomplete filling of the left ventricle in a case of cerebellar abscess on the right side. (a) Cisterna interpeduncularis; (b) cisterna chiasmatis; (x) pineal gland. Note the filling of the sulci of the convexity of brain.

concerned. Unfortunately, however, lumbar encephalography involves too many risks in cases of cerebellar abscess, so that at present the method must be strictly abandoned in spite of its clinical value.

Frequently lumbar encephalography is indicated in the following conditions: *1.* Temporal lobe abscess. *2.* Frontal lobe abscess. *3.* Malignant neoplasms of the temporal bone and paranasal sinuses. *4.* Complications simulating the clinical syndrome of a cerebral abscess. Let us consider these indications at some detail.

1. Temporal lobe abscess. There is a paucity of recorded encephalograms, but the following changes have been noted: *a.* complete or incomplete compression of the ventricles on the affected side, most often ascribable to edema of brain; *b.* dilatation of the ventricle on the normal side, for which we have as yet no explanation; *c.* lateral displacement of one or both ventricles toward the unaffected side, the displacement particularly involving the anterior part and the body of the ventricles (Cairns and Jupe[9]), while the posterior part of the cerebral hemisphere is to some extent protected against such dislocation by the strength and depth of the falx cerebri and by the union of the falx with the tentorium cerebelli; *d.* diminished filling of the subarachnoidal spaces of the convexity on the affected side.

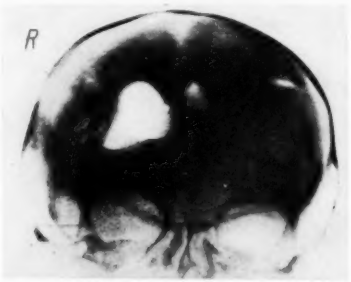

Fig. 4. Encephalogram in a case of temporal lobe abscess on the left side. Anteroposterior view.

Fig. 4 presents the anterior-posterior view of the ventricles of a case of otogenous temporal lobe abscess on the left side. The compression of the left ventricle, the dilatation of the right ventricle, the displacement of the ventricles to the right side can be seen. The subarachnoidal spaces of the convexity of the brain are not filled. The patient was cured.

Neurosurgeons particularly emphasize that in cerebral abscesses lumbar encephalography involves especial danger of producing a diffuse meningitis in addition to the other risks mentioned above; however, I could not find even one instance actually proving that danger in chronic or acute abscesses. I have performed lumbar encephalography in two cases of purulent progressive encephalitis of the temporal and occipital lobe which probably corresponds to the usual concept of an "acute" abscess. In the first patient the sub-

arachnoidal spaces were filled on both sides, but the ventricles were not filled, although 20 cc. of air were injected. In the other patient two encephalographies were made: In the first, the subarachnoidal spaces were filled on both sides, while the anterior and posterior horns on the affected side were a little compressed. In the second encephalogram, obtained after a large decompression of the skull, the difference in both ventricles was less marked. In both cases lumbar encephalography had no influence whatever upon the course of the disease.

Theoretically, I believe that in brain abscess lumbar encephalography is no more dangerous than a simple spinal puncture. As emphasized by Wartenberg,[10] we must remember that injection of air contributes toward the maintenance of pressure and thereby reduces the danger resulting from

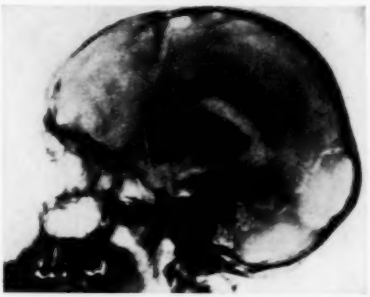

Fig. 5. Ventriculogram in a case of frontal lobe abscess. Lateral view.

the decrease in pressure caused by withdrawal of fluid. Up to the present I see no good reason to attribute a particular danger to lumbar encephalography in brain abscesses; of course, this does not imply a rejection of ventriculography in these instances, although this procedure requires a more complicated equipment and involves also definite risks.

2. There are even fewer encephalograms of frontal lobe abscesses on record than are found in temporal lobe abscesses. I have seen none; however, the experience of other clinicians proves that these cases show: *a.* compression of the anterior horn on the affected side; and *b.* dislocation of the ventricles of that side backward and toward the normal side.

Fig. 5 presents the ventriculogram of the right ventricle of a case of rhinogenous frontal lobe abscess on the right side.

The displacement of the ventricle, particularly of the anterior horn, toward the occiput can be seen. The case was operated on and cured by Meurman.[11]

3. Malignant tumors of the temporal bone and of the paranasal sinuses may involve the brain without producing definite neurologic symptoms. Encephalography is, therefore, of great aid in these instances, although one of my patients who

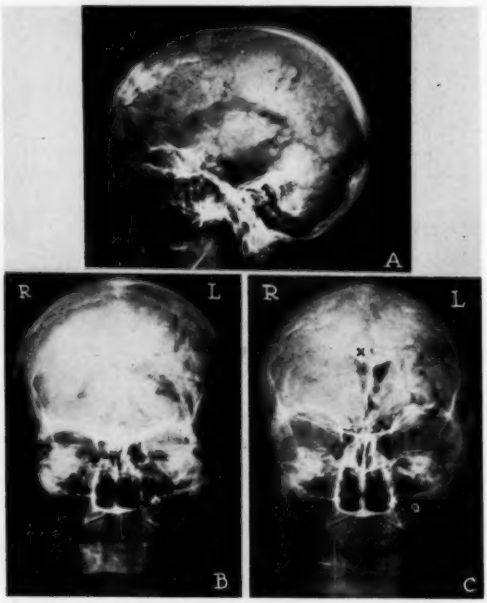

Fig. 6. Encephalograms in a case of carcinoma of the right middle ear invading the middle fossa. (A) Lateral view; (B) posterior-anterior view. Note the filling of the cella media and the suici of the convexity on the left side only. (C) Anterior-posterior view. (x) indicates the cisterna corporis callosi.

had a sarcoma of the ethmoid which involved the frontal lobe died of a hemorrhage into the tumor after withdrawal of 3 cc. of spinal fluid. In this case no air was injected. Another case concerned a woman, age 59 years, who noticed a neoplasm at the right tragus 25 years ago. On March 2, 1941, a radical mastoid operation, removal of the right concha and the squamous portion of the temporal bone was necessary on account of a squamous cell carcinoma of the middle ear. A few weeks later she had three "convulsions" and suffered

from severe headache. On July 25, 1941, lumbar encephalography was performed; 120 cc. of fluid were withdrawn and 140 cc. of air injected. Fig. 6 shows both ventricles displaced to the left and the superior and lateral edge of the right ventricle elongated. The third ventricle was dilated, the right inferior horn compressed and the subarachnoidal spaces of the convexity were better filled on the left than on the right side. These findings pointed to a marked pressure originating at the base of the right temporal lobe due to the carcinoma which had invaded the middle fossa but did not break into

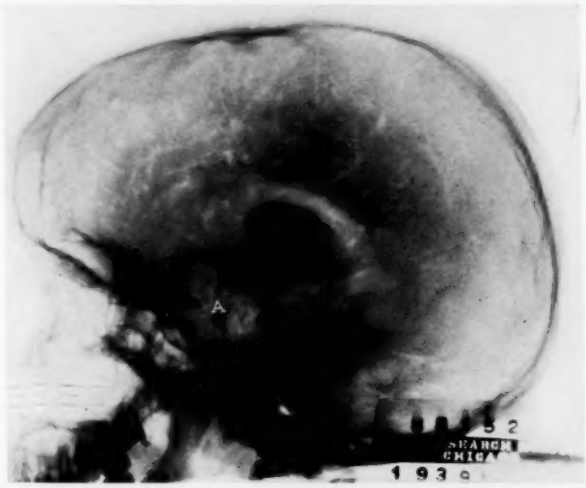

Fig. 7. Encephalogram in a case of otitic hydrocephalus, May 5, 1939. (A) indicates the marked enlarged basilar cisternae. Lateral view, right side.

the inferior horn of the ventricle. In order to ascertain the diagnosis a puncture of the temporal lobe was performed by way of the tegmen tympani and at a depth of 7 cm. tumor masses were aspirated without ill effect to the patient. She died on Sept. 26, 1941. No autopsy was made, but prior to death she had a partial paralysis of her left arm and leg and hemorrhage from the tumor mass.

4. Encephalography is of greatest importance where an intracranial complication produces symptoms resembling a brain abscess. In these cases an encephalogram taken at the proper time may serve to prevent an unnecessary exploratory

puncture of the brain. Various types of intracranial complications must be considered. In my experience the following conditions required encephalography to clarify the diagnosis:

a. Otitic Hyrocephalus: In accord with McAlpine,[12] I prefer "toxic hydrocephalus," as the disease may be due not only to an otitis but also to infections in other organs, particularly

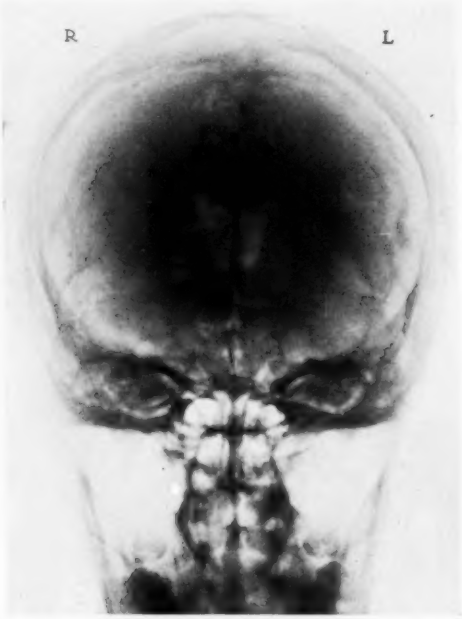

Fig. 8. Encephalogram in a case of otitic hydrocephalus, May 29, 1939. Anterior-posterior view. The ventricles slightly dilated. The third and the fourth ventricles can be seen.

in the upper respiratory tract. There are on record only very few cases of toxic hydrocephalus particularly of otitic origin in which air was injected. The findings vary. The subarachnoidal spaces of the convexity are well filled or they may be filled only on the normal side, as was the case in one patient of Dinolt[13] and myself. The basal cisterns may be normal or enlarged, the latter being the case in the last-mentioned patient. The ventricles are either normal, slightly enlarged or relatively small (Guttmann,[14] Levy [15]). I found only one case of Kessler and Savitsky[16] that presented a defi-

nite communicating internal hydrocephalus; however, it is not clear whether or not the hydrocephalus existed prior to a sphenoiditis and mastoiditis from which the patient suffered. Apparently the clinical syndrome of toxic hydrocephalus may be due to different causative factors such as external hydrocephalus, brain edema, internal hydrocephalus, which pathologic changes can also be produced by intense application of X-rays to the brain of young animals.[17] In any event, these conditions differ markedly from the encephalographic findings obtained in temporal or frontal lobe abscesses and, therefore,

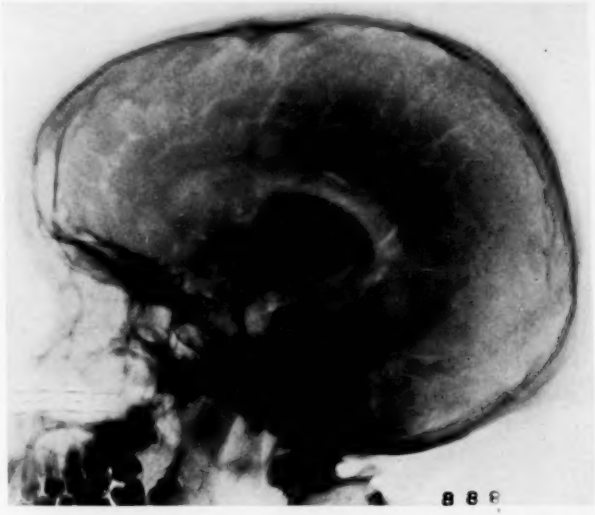

Fig. 9. Encephalogram in a case of otitic hydrocephalus, May 29, 1939. Lateral view, right side.

aid in distinguishing a brain abscess from toxic hydrocephalus.

b. Intermittent Purulent Meningitis: This form, which was first described by Brieger, affects the convexity of brain more than the base, and is clinically characterized by the appearance of focal symptoms of the brain convexity and by a chronic intermittent course. On account of the clinical symptoms it happens that in these cases a brain abscess is suspected and an unnecessary puncture of the brain is carried out. In one case of that type I injected air through a suboccipital puncture and obtained a normal encephalogram, thus

excluding a cerebral abscess. The diagnosis was confirmed by the autopsy.

c. Osteomyelitis of the Skull: It has often been emphasized that in this infection abscesses of the frontal lobe may develop without conspicuous symptoms, while general symptoms of a brain abscess such as drowsiness, intense headache, leucocytosis, nausea may occur due to external pachymeningitis

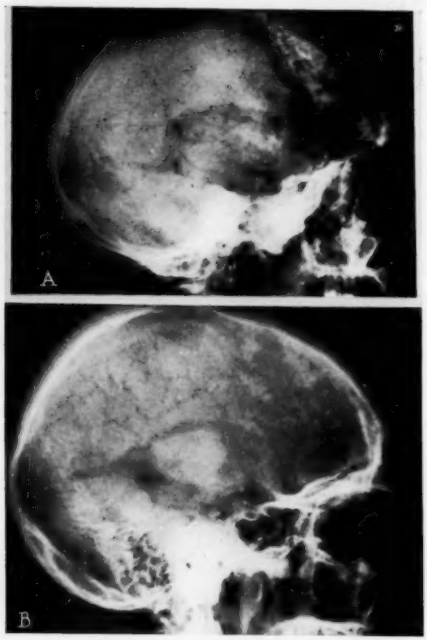

Fig. 10. Normal encephalograms in two cases of osteomyelitis of the skull.

and not a cerebral abscess. In these cases encephalography is of great help. In two cases, I have observed normal encephalograms after lumbar puncture and thereby prevented useless punctures of the brain. One of these cases (see Fig. 10A) acquired an acute spreading osteomyelitis following an endonasal ethmoid operation. The patient died from a meningitis originating in the temporal bone. The other patient (see Fig. 10B) suffered from a chronic osteomyelitis. The patient recovered after resection of the frontal squama.

It is obvious that in these cases lumbar encephalography is more advisable than ventriculography, as the latter involves an injury to the skull. For this reason I do not agree with some neurosurgeons who even in like conditions advocate ventriculography.

The presented view is by no means an exhaustive study of encephalography in otolaryngology, not even in intracranial complications. For such a purpose the material at our disposal is far too limited; but it is my aim to stimulate the interest of the otolaryngologists in encephalography because it will increase our practical and theoretic knowledge of various affections of the brain associated with diseases of the ear and nose.

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MYCOSIS OF THE MIDDLE EAR AND MASTOID.*

DR. JOHN J. SHEA, Memphis.

Mycotic infections of the middle ear and mastoid are more frequent than the American literature of otology would indicate. During the past 10 years, our attention has been recalled to the pathology and treatment of mycotic infections of the external ear by Searcy,[1] Whalen,[2] Gill[3] and others. Only casual reference has been made concerning the possibilities and characteristics of mycotic infections extending into the middle ear and mastoid (Chisolm,[4] Sutton,[4] Enlows,[5] Bristow[6] and Trexler[7]). In contrast to the teaching that multiple perforations of the membrana tympani are usually tuberculous, it is my experience that multiple perforations occur more frequently in mycotic infections of the middle ear than in tuberculosis. The presence of fungi in a culture taken from the middle ear or mastoid is not decisive proof that the pathology is the result of a mycotic infection. It may be considered positive when the accompanying clinical manifestations are those of mycosis. Its etiological significance is assessed by *1.* the clinical picture suggestive of mycotic infection; *2.* the type of fungus isolated; *3.* response to fungicidal agents; *4.* special elaborate specific tests as skin allergic responses and serological reactions. The inaccessibility of direct medication to these infections prevents their eradication and for a cure it is necessary to combine systemic medication and desensitization by inoculation with strenuous local therapy to exterminate the mycosis.

Incidence: During the summer months we treat daily mycotic infections of the external ear, but during the past five years the pathology encountered in four cases of mastoiditis and two of middle ear infection was unusual. In each instance the laboratory findings were that of a fungus. In two of the mastoiditis cases aspergillus niger was isolated and the other two were reported as nocardia. Oidia predominated in the two middle ear patients.

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PATHOLOGY.

Multiple perforations of the drum occur in the majority of instances and are seldom marginal. Through the majority of these perforations small polyps protrude, especially during the period of healing. At times these polyps become a hindrance by obstructing the avenues of entrance for direct medication. The mycotic drum is gray, thickened and less sensitive than normal, allowing of considerable manipulation without pain. Upon opening the drum, the membrane of the middle ear will be found to be swollen, with obliteration of the middle ear cavity. When the mastoid cortex is removed the appearance of the process is characteristic; the mastoid cells being filled with a pigmented fungus growth offering a contrast to the yellow bony walls. The coalescence is not constant or consistent and in areas of long duration the lining membrane will be polypoid. The progression is slow and in four of the cases operated upon was limited to the confines of the pneumatic spaces. When a radical mastoid cavity becomes a "swill barrel," its contents are a perfect media for the growth of fungi, especially in the warmer climates.

Mycology: The accepted classification of Smith[8] will be followed in this presentation.

I. Yeastlike Fungi.
   1. Saccaromytes.
   2. Monilia.
   3. Torula.
   4. Endomycete.
   5. Geotrichum (oidium).
   6. Blastomycete.
   7. Coccidioides immitis.
   8. Sporothrix.

II. Moldlike Fungi.
   9. Aspergillus.
   10. Penicillium.
   11. Mucor.

III. High Bacterial Forms.
   12. Actinomycete.
   13. Nocardia.
      a. Acid-fast.
      b. Nonacid-fast.

The diagnosis by direct smear is hazardous and by culture in Sabourraud's media is tedious, requiring at least three weeks for verification. Testing by skin sensitivity is rapid and practical, but uncertain and not scientific. Symbiosis of fungi and bacteria varies according to the stage of the infection. During an acute purulent otitis media the bacteria will outgrow the fungus and the profuse discharge washes away the contamination. But during the chronic stage the lack of flow and stagnation invites proliferation of the fungus. In the six cases reported smears were made for tubercle bacilli and cholesterin crystals with negative results.

TREATMENT.

Potassium iodide, thymol and sodium benzoate are the drugs of choice for systemic medication. Solutions or salves of these three are the best fungicides. A solution of bismuth violet may be injected with good results and its color serves to illustrate its distribution. Cresatin, silver pictrate and solutions of copper sulphate are of value. The most potent local therapy is obtained by melting a salve of acid benzoic 12 per cent, acid salicylic 6 per cent and chlorthymol 0.25 per cent and instilling it into the middle ear and external canal while in the liquid state. Fortunately, the melting point is low enough not to blister and precautions should be taken to prevent the formation of air bubbles and pockets between the salve and lesion (personal treatment of Dr. Charles D. Blassingame). At the suggestion of Walsh, "propylene glycol" has been used as a vehicle for the above because of its ability to permeate. Apparently, the sealing off of the middle ear is of value. In the beginning, the ointment should be changed every second or third day and for its removal suction through small glass pipettes is efficacious and painless. As the infection subsides, the interval of changing may be lengthened to five days.

Chemotherapy apparently controls the amount of discharge, but has not eradicated any of the stubborn mycotic infections. This may be explained by the fact that chemotherapy diminishes the bacterial element of the symbiosis.

CASE HISTORIES.

Case 1: N. H., age 13 years, had a discharging right ear for three years with a moderate sized perforation in the center of the drum. At operation the mastoid process presented a mottled greenish-yellow appearance. The discharge during convalesence had the characteristic fungus odor and the culture was reported as aspergillus niger. Repeated smears were negative for tubercle bacilli and cholesterin crystals.

In spite of local and systemic therapy, the ear continued to discharge a black pigmented pus for a year, except when daily cleansed and medicated.

Case 2: C. M., age 12 years, acquired a mycotic infection of the external auditory canal from swimming, which progressed and became a middle ear infection without pain or fever. The perforation was through Shrapnell's membrane. The discharge presented the characteristic black pigment of aspergillus niger and resisted local extermination. A polyp protruded through the perforation during the fourth Spring. For a time the discharge was controlled by a series of inoculations of a vaccine of aspergillus niger, trichophyton and oidia. To increase her immunity to the purulent infection she was given staphylococcus and streptococcus

antigen. Two years later, during an acute cold, the mastoid became surgical and a semiradical mastoid operation was performed. At operation the antrum, aditus and middle ear were found to contain a black pigmented debris which when evacuated left a cadaveric type of bone devoid of membrane. Neoprontosil therapy did not influence the infection but sulfathiazol was effective and the discharge temporarily ceased, to return one month later. A saturated solution of potassium iodide — 10 minims three times a day — was administered and controlled the amount of, but failed to eradicate, the discharge. Apparently a radical

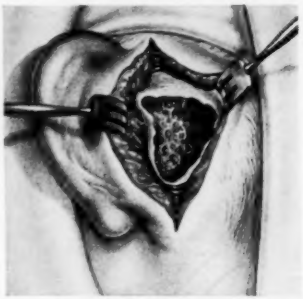

Fig. 1. Case 1. Mastoid cells presented a mottled, greenish-yellow appearance.

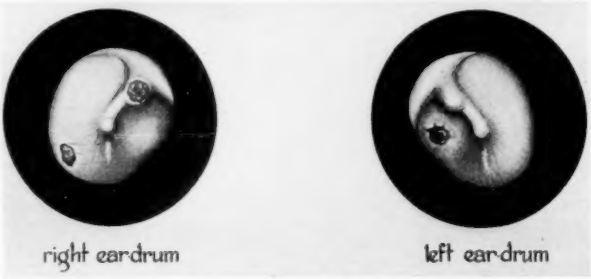

Fig. 2. Case 4. Two perforations of right drum not marginal.

mastoid operation will be necessary to expose the infected areas for direct medication before a cure can be anticipated.

Case 3: I. H., age 50 years, developed a fungus infection of the external and middle ear which extended into a previously operated mastoid cavity. The middle ear, aditus and antrum contained a black pigmented discharge and a semiradical mastoid operation was performed. For a time healing was uneventful, but two months later the external ear became reinfected and in spite of strenuous local and systemic treatment, a sinus developed into the superior petrous cells. Chemotherapy of neoprontosil will control the discharge but, as in the preceding case, a radical mastoid operation has been advised to remove the recesses which are infected. The culture taken three and one-half years after operation was reported as being nocardia, proteus and staphylococcus aureus.

Case 4: E. B., age 18 years, had a bilateral O.M.P.C. and mastoiditis with two perforations of the right drum. The discharge had the foul odor characteristic of fungus contamination. A culture and smear were reported as positive for nocardia. Roentgenograms revealed an arrested type of mastoid development. At operation the cells were filled with granulations and a caseous material. The membrane of the antrum and aditus was polypoid. The convalescence was protracted and required the administration of potassium iodide for months with local therapy of many of the fungicides before the contamination was eradicated.

Case 5: S. K., age 19 years, has had since 1938 a bilateral fungus infection of the middle ear which can be controlled by local cleansing and desensitization with oidia, staphylococcus and streptococcus. This lad has been treated by several qualified otologists and among the remedies used have been formaldehyde, allantoin and urea, cresatin, iodoform in oil, silver picrate and benzosalicylic compound. A deep atresia of the canals has been present since his first examination and limits the thoroughness of cleansing of the deeper recesses. Surgery has not been advised because of the poor prognosis and the absence of any present danger to his life.

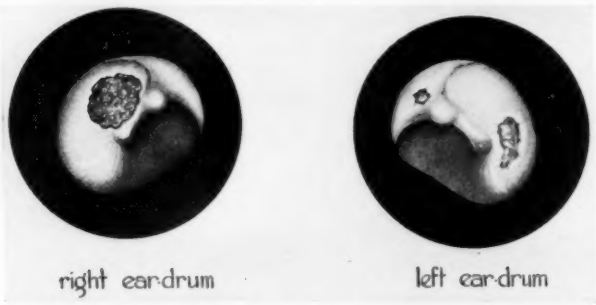

Fig. 3. Case 6. Two perforations of left drum, not marginal.

Case 6: C. J., age 22 years, while being observed for an allergic Eustachian salpingitis developed a silent otitis media which perforated through the center of the right drum. The discharge was scanty, with a tendency for a scab to cover the perforation. Because of the painless perforation the secretions were unsuccessfully studied for tubercle bacilli. Physical examination and Roentgenological study of the lungs failed to substantiate any tendency towards a tuberculous infection. The lad was kept under semiweekly inspection and a month later, the left ear had a silent infection to be followed by a second perforation. The clinical picture being that of tuberculosis, he was again restudied and the only positive laboratory finding was that of a constant fungus growth (monilia oidium and aspergillus). Many fungicide preparations have been tried, but the only successful control of the discharge has followed the instillation of a liquid unguentum of benzosalicylic compound.

ALLERGY.

Allergic individuals when infected by fungi are prone to chronicity, because they become sensitive to the fungi instead of building up an immunity. In the treatment of mycotic

conditions of the middle ear and mastoid of allergic individuals it is necessary to desensitize them against the offending fungi.

CONCLUSIONS.

1. Mycotic infections of the middle ear and mastoid are not infrequent, but resist the most careful therapy.

2. Multiple perforations of the drum are more frequently of mycotic than of tuberculous origin.

3. Only radical mastoid surgery appears sufficient to eradicate a fungus infection of the mastoids.

4. Allergic individuals are prone to mycotic infections.

At early meetings of the American Otological Society the treatment of mycosis was presented. George Strawbridge, of Philadelphia, in Volume 2, Part 2, Page 254 of the Transactions of the American Otological Society reported the use of sodium salicylate for the treatment of Aspergillus niger. John Green, of St. Louis, in 1870, reported a case of Aspergilli in the external auditory meatus.

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IMPAIRED HEARING IN SCHOOL CHILDREN.*†‡

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Our report[1] to this Society two years ago, based on the examinations of 1,365 white children, 8 to 14 years of age, attending regular classes in Baltimore schools, showed that the most common hearing defect in children is impairment of thresholds for some or all of the tones above c^4; *i.e.*, for frequencies higher than 2,048 cycles per second. Nearly 40 per cent of the children had such impairments. Only about 3 per cent of the children had impaired hearing for all tones or difficulty in understanding the spoken voice.

The examinations of these children also showed that regeneration or regrowth of lymphoid tissue in the nasopharynx often occurs after adenoidectomy. Lymphoid tissue is an integral part of the mucosa of this region, and all of it cannot be removed even by the most meticulous operation without endangering the patency of the Eustachian tubes by scar tissue formation. The mucosa that grows out over the operative wound, therefore, contains lymphoid tissue, and this may again undergo hyperplasia with infections of the upper respiratory tract. Slightly over half of the children had had a tonsillectomy and adenoidectomy before we first examined them, but a majority of these operated children had large adenoid masses or hyperplasia of the lymphoid tissue in the fossa of Rosenmüller and in the region of the nasopharyngeal orifice of one or of both Eustachian tubes. Nearly three-fourths of the unoperated children had similar conditions.

During the past two years a group of these children has been treated by irradiation of the nasopharynx, after the method described by Burnam.[2] They were selected for treatment because they had impaired hearing and lymphoid over-

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growth of the tubal orifices, as determined by examination with a nasopharyngoscope. Most of them also had opaque and retracted tympanic membranes. Treatment was advised for 239 children and actually started on 208. Of these, 152 have been followed over the two-year period and have had from eight to 12 re-examinations each, including one or more since September, 1941. A total of several hundred other children, who are clinic or private patients of our associates, have also been treated with radon. The results obtained with those who have returned regularly for re-examination and treatment have been similar to the results to be reported today for the specially selected group of school children.

The idea underlying the treatment may be summarized as follows: Large adenoids or lymphoid nodules near the nasopharyngeal orifice of the Eustachian tube interfere with normal ventilation of the middle ear. This interference with the normal ventilation results, by absorption of some of the contained air, in a middle-ear pressure chronically less than atmospheric. The pressure difference itself may cause a slight impairment of hearing as well as retraction of the tympanic membrane, but the important result is mucosal hyperemia and edema. If the condition persists, mucosal hyperplasia and fibrosis develop. The mucosal changes, together with the exudate and transudate that accumulate in the middle ear, interfere with the transmission of sound waves to the inner ear. In contrast to the classical idea of the effect of catarrhal otitis media on hearing, we find that the perception of high tones, rather than of low tones, is usually impaired first. Probably this fact was not observed sooner because until the advent of good audiometers 2,048 was the highest frequency for which the threshold was routinely determined. With the Galton whistle or the monochord the differentiation is only "heard" or "not heard." The impairments begin with tones of a frequency above 2,048, usually above 4,096 cycles per second. At this stage children have no difficulty with voice and tuning fork tests. The treatments have been based on the idea, therefore, that restoration of normal ventilation of the middle ear at this early stage will arrest the process and prevent the formation of lesions severe enough to interfere with the transmission of the important conversational tones.

Spontaneous regression of adenoids frequently occurs during the prepubertal and pubertal period of life. To evaluate

approximately the possible rôle of this factor in the treated children, a control group was selected. The basis of selection was: The presence of nasopharyngeal conditions similar in appearance, on examination with a nasopharyngoscope, to those in the children to be treated, but the hearing either good or only slightly impaired for the high tones. The ideal method of selection, for control of the experiment as such, would have been to divide the children for whom treatment was advised into two groups by chance. Because we were dealing with children, not with experimental animals, treatment was urged for all with tubal overgrowth and impaired hearing of more than a slight degree. Also, 12 children in the control group whose hearing became markedly impaired while under observation were advised to have treatment. The group is, therefore, good for a control on the factor of spontaneous regression, but it is not good for use as a control on the hearing changes in the treated children.

Three hundred thirty-seven of the untreated children have been re-examined since September, 1941; with a few exceptions this was the fifth examination for each of them in the two-year period of observation. In 106, or 31 per cent of these children, spontaneous regression of lymphoid tissue has occurred to such an extent that both tubal orifices are now normal in appearance. In about 15 per cent more there has been definite regression of lymphoid tissue, but one or both tubal orifices are still partially overgrown. Fluctuation in amount of the nasopharyngeal lymphoid tissue has occurred in about half of these children, and at the last examination nearly 10 per cent of them had more lymphoid tissue than at the first examination.

Of the 152 children whose treatment with radon was started during the school year 1939-1940 and who have been re-examined since September, 1941, the tubal orifices are normal in appearance and the adenoids are small or absent in 136, or 89.5 per cent. Because their tonsils were badly infected, 22 of these children had an operative removal of tonsils and adenoids, supplemented by radon therapy of the nasopharynx. Only 16, or 10.5 per cent, of the treated children had enough adenoid tissue left this year that further treatment was needed. The average number of treatments was slightly less than four; only a few children have had more than six treat-

ments. One boy has been treated nine times, and his tubal orifices are still partially overgrown. No explanation has been found for the persistence of adenoids in a few children after an amount of irradiation adequate for the others.

Five of the 16 children who needed further treatment this year had had a regrowth of lymphoid tissue near the tubal orifice after it had once undergone regression. Such regrowth has also been observed in clinic and private patients. It is our impression that regeneration of nasopharyngeal lymphoid tissue occurs much less often after shrinkage by radon than it does after surgical removal, but to assure the most benefit from the treatment all children must be re-examined periodically and further treatment promptly given if indicated.

None of the children have suffered radon burns or complained of sore throats after treatment. A few of the many adults who have been treated similarly to the children, either as clinic or as private patients of our associates, have complained of pain and have experienced exacerbations of a chronic nasopharyngitis. With one exception, all children who have had a purulent otitis media since treatment was started had histories of recurrent otitis. Most of the children with histories of recurrent otitis have not had attacks since the amount of lymphoid tissue in the nasopharynx was reduced. Statements as to the frequency of colds, sore throats, etc., in past years are notoriously unreliable: in many children the number of infections of the upper respiratory tract is definitely less than before treatment, in many others the number seems about the same. The new case of otitis media in a treated child cannot be ascribed to congestion following irradiation because the infection occurred during a season when new cases of otitis were frequently being seen in untreated patients in the clinic and in the private practices of our associates in Baltimore. The balance is unquestionably in favor of radon as a useful therapeutic measure for the treatment of hyperplastic lymphoid tissue in the nasopharynx of children. It should not be used during or soon after an infection of the upper respiratory tract.

The effect of the radon therapy on hearing is more difficult to evaluate than is its effect on nasopharyngeal lymphoid tissue. In the first place, as has been pointed out already, a suitable control group is lacking. The second, and the more serious difficulty, arises from the diversity of lesions that may cause similar impairments of hearing. There is no question that the hearing of many children improves markedly as a result of the regression of middle-ear lesions after shrinkage of the nasopharyngeal lymphoid tissue, but in statistical analyses of large groups these improvements are offset by the impairments caused by progressive lesions whose course cannot reasonably be expected to be influenced by the therapy. The value of the therapy, therefore, can be better determined by methods of studying the observations other than statistical.

The changes in hearing acuity that have occurred in the untreated children are of considerable interest, even though they are not suitable for use as a control on the effect of treatment, for the reasons already stated. With a few exceptions, the hearing of each child of the untreated group has been carefully tested five times during the two years. Because these children had at their first examinations either good hearing (*i.e.*, thresholds for all frequencies within the range of normal variation for our conditions, with the exception of "tonal dips") or only a slight to moderate impairment for high tones, there was not much chance for marked improvements to occur; however, it was expected that comparisons of the thresholds at the first and at the last tests would show an illusory improvement from practice with the test. For the low frequencies (32, 64, 128 and 256 cycles per second) the averages do show slightly better thresholds in the later tests. The average of the changes for low tones is from 1.5 to 4 dcb. in the different subgroups, as divided for study on the basis of sex and age, and the lower the frequency the larger is the average improvement. It may be possible that the shrinkage of the mucosa of the nose and nasopharynx on five occasions in two years, preparatory to examination with the nasopharyngoscope, had a beneficial effect, but probably practice with the test is the more important factor. That the apparent improvement was not greater than this speaks well for the reliability of the first tests of thresholds of hearing that can be secured with children when examined alone in quiet

surroundings. For the middle range of frequencies (512, 1,024, 2,048 and 2,896 cycles per second) the average change in two years was less than 1 dcb. for all subgroups, an amount certainly without significance except as an indication of the reliability of the tests.

For the high frequencies (4,096, 5,793, 8,192, 10,321, 13,004 and 16,384 cycles per second) the average impairment at the last test was greater than at the first test. Practice with the test, of course, cannot explain this change, and unreliability of tests cannot explain it, in view of the reliability of these same children for other frequencies. The best explanation seems to be that the children were two years older at the last than at the first test, and that, therefore, the various lesions that cause impaired hearing for high tones had had more opportunity to exert their effects on hearing acuity. For the boys the change averaged over 2 dcb., for the girls less than half that amount. Both the age and the sex differences are in agreement with the observations we reported two years ago with respect to the first examinations of the entire group of 1,365 school children. At these first examinations impaired hearing for high tones was found to be present more often in boys than in girls; also, for each sex, impaired hearing for high tones was present more often in the children 11 to 13 years old than in those 8 to 10 years of age. It is of interest to note that all of these observations are in good agreement with those reported by Bunch and Raiford[3] and by Ciocco[4] on sex and age differences in the hearing acuity of adults, and with those recently reported by Ciocco and Palmer[5] for children.

A seasonal difference in the incidence of impaired hearing for high tones was noted at the first examinations of the 1,365 children and was mentioned in our report of two years ago. Comparisons of the repeated examinations of the untreated children reveal a seasonal fluctuation; for the group as a whole the hearing is worse during the season when upper respiratory tract infections occur most commonly. The effect is less clearly evident in the treated children. A special study of these seasonal fluctuations has been made by one of the members of our group, Dr. Robbins, and will be published elsewhere.

The large series of repeated examinations has afforded observations of interest with respect to changes in "tonal

dips." Some of the dips have disappeared, some have remained essentially stationary, some have shown fluctuation, and some have progressed either for the one frequency or to include adjacent frequencies. Dr. Loch is making a special study, to be published elsewhere, of the "tonal dips" of the material.

Consideration of the changes in hearing that have occurred in the treated children can best be done by dividing them into two groups: *1.* Those who at the first examination had impaired hearing only for some or all of the high tones; *2.* those who had, with one or with both ears, impaired hearing for more than the high tones and difficulty understanding the spoken voice in otherwise quiet surroundings. The first is much the larger group, and the boys in it outnumber the girls more than three to one. The clinic and private patients who have been treated because they had impaired hearing for high tones and an excessive amount of nasopharyngeal lymphoid tissue show a similar discrepancy in the proportion of boys to girls.

It was recognized from the first that some of the children with impaired hearing for high tones doubtless had lesions other than ones secondary to tubal occlusion by excess lymphoid tissue. Nevertheless, treatment was advised; and even yet with new patients in whom we are fairly certain that most or all of the impairment is caused by an atrophy of the nerve, or of the nerve and end-organ, in the basal turn of the cochlea, treatment is advised if the nasopharynx is not entirely normal in appearance. Such children should be given the benefit of any doubt in the diagnosis and the nasopharynx should be treated in order to decrease the danger of having a progressive conductive lesion superimposed on the cochlear lesion, if there proves to be one. In many cases the diagnosis can be established only by the therapeutic test.

The proportion of the children with impaired hearing for high tones for whom the therapeutic test indicates a progressive atrophy in the basal turn of the cochlea is much larger than was previously supposed. Slightly over one-third of the ears that had impaired hearing for some or all of the high tones at the first test have had the impairments increase during the two-year period of observation, in spite of regression of adenoids and other nasopharyngeal lymphoid tissue

until the region of the orifice of the Eustachian tube is normal in appearance, as observed with a nasopharyngoscope. This has happened also with the clinic and private patients. Some other lesion may be responsible for a few of these progressive impairments, but the most probable explanation for most of them is a progressive atrophy of the nerve, or of the nerve and the organ of Corti, in the basal turn of the cochlea. This interpretation, if correct, sets back into childhood the age at which such lesions commonly may develop, lesions which have usually been regarded as of frequent occurrence only in adult life. These are the cases which in the averages of groups, also in other statistical analyses of the observations, offset the improvements in hearing that occur in the ears whose impairments were caused by middle-ear lesions that regressed after treatment, in accordance with the idea underlying the therapy. Is it fair, in an evaluation of the therapy, to count them as failures? We believe not, because the treatment will prevent many of these children from having a so-called combined deafness later in life. The nerve deafness caused by an atrophy limited to the basal turn of the cochlea, as most cochlear atrophies are,[6] does not materially handicap a person in most social and economic activities. In only a very few vocations is good hearing for the frequencies above 2,048 cycles per second necessary for success. Difficulty in understanding conversation in a crowd is the chief complaint of people with such hearing defects; but when there is added to the high-tone loss even a moderate impairment of the thresholds for middle and low tones, the individual is severely handicapped in the activities of daily life, and if a child, he or she has great difficulty acquiring an education. We believe, therefore, that it is important to do everything possible to prevent the development of middle-ear lesions in a child with an inner-ear type of impaired hearing.

Hearing acuity for high tones definitely improved in about one-third of the ears with hearing defects limited to this range of frequencies. Sometimes the improvement began soon after the treatment was started, sometimes it did not occur until the tubal orifice had been normal in appearance for several months. Tubal inflations have not been used; perhaps they would have hastened the appearance of improvement in hearing acuity for some of the patients. The results warrant the conclusion that the impairment for high tones in these

ears was caused by middle-ear lesions that regressed after treatment of the nasopharynx had favorably influenced ventilation of the middle ear. Without question these children have been benefited by the treatment. Probably the benefit is of a degree greater than is measured by the improvement in thresholds for high tones, because further deterioration of hearing from the middle-ear lesion has been prevented.

The amount of impairment was essentially the same at the last as at the first test in slightly less than one-third of the ears that had impairment for high tones only. For most of these cases the diagnosis has to remain uncertain: the cause of the impairment may be either a stationary inner-ear lesion or an irreversible middle-ear lesion. Evaluation of the effect of the therapy by the method of averaging the changes in hearing thresholds would show no benefit for such children. Actually, those with inner-ear lesions have had the danger of a combined deafness lessened, and the others have had potentially progressive middle-ear lesions arrested.

For the entire group of treated children who had impaired hearing for high tones only, there has been an average change for low tones similar to that which occurred in the untreated children. As with the latter group, the changes consist of shifts in response within the range of normal variation of thresholds, and may well be only the effect of experience with the test. For tones of the middle range of frequencies also, the individual changes are small and the average change is, as in the untreated group, less than 1 dcb.

Among the children who were attending regular school classes, and who had poor hearing for tones other than the high ones, the common type of impairment was that with thresholds for the low and middle tones down 25 to 40 dcb., and for the high tones somewhat more. With impairment greater than this for the better ear, children seldom can stay in the regular classes. Thirty of the 38 children in regular classes who had impaired hearing for the spoken voice either had a purulent otitis at the time of examination, a history of otitis or scarred tympanic membranes. Among the clinic and private patients with similar hearing losses — and there are many more in this part of our material than in that selected by examination of regular school children — the proportion of deafness apparently caused by otitis media is also high.

As a group, these are the children who derive the most immediate benefit from radon therapy. Many of them have had improvements of from 15 to 30 dcb. for all except the very highest tones. Such improvements restore the hearing to essentially normal for all practical purposes, and from an educational standpoint such children cease to be special problems.

Most of the children of this group whose hearing does not improve have either a chronic suppurative otitis media or extreme middle-ear lesions from previous repeated attacks of otitis. Even though the nasopharyngeal conditions are restored to normal and the suppuration is stopped by suitable local treatments, permanent damage to the middle-ear structures has already been caused. Hearing acuity may improve slightly, but not to an extent sufficient to be of much immediate benefit either to the child or in the educational problem created by his hardness of hearing.

From our experiences with such children we are convinced, and we are sure all otologists will agree, that a very large number of cases of handicapping degrees of deafness could be prevented annually, in this country alone, by prompt medical care of all new cases of acute otitis media. Promptly and properly treated, acute otitis media soon subsides without, in most cases, leaving any impairment of hearing.

All otologists are familiar with the serious conditions that may and often do develop when acute otitis media is neglected; it is not necessary even to list them now, but we do wish at this time to point out most emphatically that the need for prompt medical care of acute otitis media in children is not realized by most people.

The general public does not know that no method of therapy can remedy the damage that results from neglect of these children. We believe that lay organizations, such as leagues of the hard-of-hearing, service clubs, etc., desirous of helping to prevent deafness but uncertain how to proceed, could be of great assistance by campaigns of education of the adult public, particularly the parents, teachers and school nurses. Such organizations can materially help to prevent deafness in their communities if they will insist that educators and

health officers stress the importance of prompt medical care for all children with acute otitis media. Radium is not needed for the proper care of this condition, only rarely are the services of an otological specialist needed to bring about satisfactory healing of acute otitis media, and an audiometer is not needed for the discovery of the children who need treatment. The possibility of success in such a campaign is, therefore, not limited to the larger communities, nor to those with special equipment and personnel. By a nation-wide campaign of the type suggested, we believe more deafness can be prevented during the next 10 years by people not specialists than will be cured by the personal activities of all otologists now in practice. All too often the deafened person first goes to see an otologist after it is already too late to restore the hearing by any method of treatment. The general public should be taught to think of most deafness as a preventable disease, not as a condition for which a specialist should be consulted after the damage is done.

Children whose better ear has an impairment for middle tones of more than 40 dcb. have great difficulty in the ordinary classroom and are usually put in special classes or schools. For that reason very few with impairments greater than this were discovered or treated as a result of our examinations of children in regular classes, but many of the children who have come as clinic or private patients have the more severe degrees of hearing impairment. Most of these children, of course, have some form of congenital or hereditary deafness, for the lesions of which no treatment is effective. Mumps and meningitis are also common causes of these severe impairments. For all of these children who also have an excessive amount of nasopharyngeal lymphoid tissue treatment is advised as a prophylactic measure to lessen the danger of having a middle-ear lesion superimposed on the primary cause of the deafness, not with the expectation that the treatment will materially improve the hearing. Some of these children have had slight improvements of thresholds, not enough to change the methods needed for their education. In only a very few cases has the therapeutic test indicated that the severe impairments were caused entirely, or almost entirely, by middle-ear lesions secondary to tubal occlusion by adenoids. Audiograms and histories of two of these cases were included in the paper by Crowe and Baylor[7] in 1939.

These children have retained good hearing, but such almost miraculous recoveries should not be expected often.

The condition of the teeth of the 1,365 school children, as was reported two years ago, was not significantly related, statistically, to the acuity of hearing at the first examination, nor was the height, the weight or any of several other anthropometric observations made. Likewise, none of these items seems to have affected the changes in hearing or in the size of the adenoids that have occurred during the period of repeated examination, either in the treated or in the untreated children. Although negative, these facts are of interest and a separate report about them will be published by Dr. Langer, who has analyzed our observations with respect to these relationships.

DISCUSSION AND CONCLUSIONS.

What practical conclusions can be drawn at the present time about procedures that will help prevent deafness in children?

In the first place, fight acute otitis media. The importance of doing this has already been discussed and there is general agreement that much deafness can thus be prevented. This conclusion, therefore, does not need further elaboration now. The next step is to organize educational campaigns that will give physicians a chance to treat all cases of acute otitis media promptly.

The second practical conclusion is that radon is a useful addition to methods for reducing the size of hyperplastic lymphoid masses in the nasopharynx. Irradiation with radon, or with radium, is certainly the simplest method by which the size of adenoid masses can be controlled, either before operation or after a regeneration following operative removal. Until recently it was an expensive method except in a few localities where radon was available at a reasonable price. A few months ago one of the large radium companies announced that it will rent an applicator containing 50 mg. of radium for $15 a month, or 100 mg., divided between two applicators, for $25 a month. At this price for the radium it is

practicable to make irradiation treatment the cheapest as well as the simplest method in any community that has a capable otologist. If only 15 or 20 patients a month are treated the cost of the radium becomes the smallest part of the expense incident to any organized effort to prevent deafness. Twenty-five dollars a month means only $300 a year, an amount certainly practicable for the health department or school budgets of even small communities. No longer is it necessary to have a large investment tied up in radium in order to utilize this method of treatment.

The third practical conclusion is that it is possible to restore the hearing of many children with impairment for conversational voice and thus to simplify the educational problem for them, for their parents and for their communities. Over the country as a whole the total number of such children is large, and it should be kept in mind in planning programs that these are the children for whom the most immediate benefit can be expected from treatment. To locate or discover these children it is not necessary to have an audiometer, not even a phonographic audiometer, so that priorities in favor of military materials need not stop this part of any program anywhere. Such children can be picked out of any group by simple tests that anyone with common sense, a watch and a voice can make. The results of tuning fork tests are of interest, but we have found that a prognosis of the effect of treatment on hearing cannot be based on them. Some children with extremely shortened hearing by bone conduction have made excellent recoveries, and hearing by bone conduction has returned along with hearing for air conduction. The decision to treat should be based on the combination of impaired hearing and hyperplastic lymphoid tissue in the region of the nasopharyngeal orifice of the Eustachian tube. If audiometers are available they should of course be used, providing it is well understood that testing with an audiometer, either a phonographic or a pure-tone model, is a far from infallible method of determining the hearing acuity. Very often, indeed, audiometers are used without due regard for the sources of erroneous results. Many audiometers in use are considerably off of correct calibration, many are used in noisy surroundings and many are operated by people who have not been trained in their proper use. No matter what method of group testing is employed, individual re-examinations should be made of all children who fail the group test.

Fourth: What can be done, of a practical nature, for the children whose hearing for the spoken voice does not improve after thorough and careful treatment? Our experiences have convinced us that the duty of the otologist does not end with that decision. He should explain to the parents what modern wearable hearing aids can do to help their child, and tell them that an aid will not only help him hear but that it will also help him learn to speak clearly, to get an education and to develop a normal personality. Most parents do not realize these facts; even many apparently intelligent parents. The otologist should, therefore, insist that the child deserves this chance, see to it that he gets a suitable aid and that he uses it, learns how to take care of it, etc. Many of you will protest that much of this is not the physician's duty, and we agree; but in many communities, including large ones as well as small, it will be necessary to educate the educators before these aspects of the task can safely be delegated to them.

Finally comes the question of doing something about the children with impaired hearing for high tones only. There are without doubt more of them in every community than there are of children with other forms of impaired hearing, but they are also the most difficult to locate and as a group the results that can be obtained by any method of therapy are the least noticeable at the time. We believe that it is worse than useless, in fact definitely harmful, to try to find these children in any community *until* preparations are made to do something for them when they are found. Our attitude is: *If* a good audiometer is available, and *if* there is a budget sufficient to have the audiometer *properly* used by a trained examiner, and *if* there is a good otologist who is willing to make the physical examinations of the ears, nose and throat of each child and to treat large numbers of them and re-examine them periodically for years, *then, and* NOT UNTIL THEN, is it wise or practical to start the search for the children with hearing losses for high tones only. There is no doubt that the results from a carefully carried out program such as suggested will be well worth the effort and the expenditure; but do not expect the results to be spectacular, because neither parents nor teachers will have previously realized that these children did not hear perfectly, and they will not notice the change even in those who have the most improvement for the high tones. Preventive medicine seldom is spectacular, and this aspect of it is not one of the exceptions.

In the final sentence of our report two years ago it was pointed out that the prevention of impaired hearing in children is a problem of such magnitude that for its practical solution widespread co-operation of many types of individuals will be needed. The further observations we have reported to you today and the opinions we have expressed will serve, we hope, to encourage many individuals to undertake practical programs for the prevention of deafness among the children of their own communities. Each such program, to succeed, must be carefully planned and must be adapted to the personnel and the facilities of that, not of the ideal, community.

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VITAMIN THERAPY TODAY.

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Decorating the entrance hall of the Cornell Medical School in New York are four plaques. They sum up the entire history of Medicine: "Sixteenth Century, Anatomy, Vesalius." "Seventeenth Century, Physiology, Harvey." "Eighteenth Century, Pathology, Morgagni." "Nineteenth Century, Bacteriology, Pasteur." Should we not now add "Twentieth Century, Nutrition"?

Not only has the study of the "intake" of human and other animals, and also of plants, made greater strides in the past 20 years than throughout all history, but it seems probable that before this century closes the human race will become stronger and more healthy than ever before — provided we can and shall abide by the new-found laws of nutrition. We can, if good food is available and there is not a terrific world shortage after this, our "War for Survival." We shall, at least in this country, if the general public becomes educated in the facts of nutrition and at last becomes aware of the difference between the silly and indiscriminate "taking of vitamin pills," as contrasted with the true values of the vitamins, especially in the foods themselves. Of course much more will be discovered; but even today the essentials are so well known that from this time on we have no excuse to plead ignorance.

If better food, properly cooked, is to improve the human race, the first and perhaps the most important consideration is the chemistry of the fetus. Like all living things the embryo requires the vitamins; in fact, only by providing the needed vitamins in an adequate amount can the mother-to-be expect to have a truly normal baby. The "embryologic approach"[1,2] to therapy is based on the following concept: Not only does the embryo require vitamins, but each germ layer makes a special demand for those particular vitamins that are necessary for its own development; the ectoderm demands "A" and the B Complex; the mesoderm demands "C" and "D"; and the entoderm demands "A" and the B Com-

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plex. According to this theory, if the pregnant woman lacks a certain vitamin, one germ layer of the embryo will be particularly affected. For example, if "D" is lacking, the mesoderm is especially deprived — and the bones of the baby, derived from the mesoderm, will be poorly developed at birth. Then throughout life, the derivatives of each germ layer continue to demand the same vitamins that meet its special needs.

If this concept proves to be correct — that each germ layer has a particular relationship to certain vitamins and not to others — we then have a rational approach to therapy. If we as clinicians note a lesion of the eye, ear, nose or throat, we know of what germ layer this particular tissue is a derivative, and so have an immediate clue as to what vitamin or group of vitamins are needed.

It is naturally impossible to determine the exact amount of each vitamin in a human body. Perhaps we will never know; available information as to storage and optimal intake of some of the vitamins gives us the only reasonable approach we have at the present time. Even now, however, we can be sure that the vitamins constitute an almost negligible part of the body weight — and yet the body cannot function without them. It has been estimated that the average adult human body contains between 3 and 5 gm. of "C." Roughly, there are 18 to 20 vitamins that are already chemically identified, or partially so. Most of the vitamins probably have a smaller amount of storage than "C." It is startling to realize what a very narrow margin there is between perfect health and a severe deficiency; for example, if the body has 4 gm. of "C" and should lose only 2 or 3 gm. of it, scurvy would be present. With most of the vitamins there is an even narrower margin between health and disease. What might a few pounds of vitamins have meant to our defenders of Bataan and Corregidor!

As to terminology, realizing that, for example, "B_1" is a chemical substance quite different from "B_2" and that "B_6" is different from either — except that they are all soluble in water — many of the leading scholars consider it advisable to discard the alphabetic terms and to use the actual chemical names — such as thiamin chloride, riboflavin and pyridoxine. Eventually, no doubt this will be and should be done; how-

ever, at the present time we have no chemical name for "A," and there is a certain simplicity in the use of the letters of the alphabet — especially because we clinicians have not yet mastered our "A, B, C's."

A survey of the contributions that have been made to vitamin literature, including comments made on them in two previous editorials,[1,2] may help us to clarify the present status of vitamin therapy, and also call our attention to the signs and symptoms for which we should be on the alert.

Our present knowledge might now be classified in a reasonably definite manner, under four headings: *1.* What are the facts upon which we can rely; *2.* What is probably to be relied on; *3.* What is possibly to be relied on, and *4.* What is improbable. The following resumé of the clinical experience of those who have studied the effects of vitamins on the eye, ear, nose and throat incidentally gives us the opportunity to check on the accuracy of the embryologic approach to therapy.

RELIABLE.

First we will consider the general facts that are now known; and then the disturbances of the eye, ear, nose and throat for which vitamins have been successfully prescribed.

1. Inadequacy of diet all over the world. In our own country it appears that the main lack has been, and still is, in the B Complex. As a side issue, perhaps the most striking observation that has been made following B Complex therapy has been the relief of constipation. These vitamins have been tried for various conditions, with or without result, but the patients themselves have commented on the resultant bowel movements. As one patient expressed it, "What is that excellent laxative contained in those vitamin tablets?" Constipation is such a common complaint in our country that it now seems reasonable to assume that it is often due to an inadequate supply of the B Complex in the national diet.

2. Faulty methods of cooking, throughout the world. Realizing that the mere prescribing of vitamins cannot compare with a well-balanced full diet, we may prescribe the proper foods — only to have them depleted of vitamins and minerals by improper cooking. In this country, the miller first "refines" most of the vitamins out of the wheat, giving

us an impoverished flour — and then the cook boils or fries away some more of them — leaving little of these essentials to a proper diet. The correct methods of cooking are now well known — in fact, all we need to do now is to adopt and use them.

3. No deficiency, no cure.

4. When a lesion is due to a deficiency, vitamin therapy is specific.

5. Evidence has accumulated that we should usually not rely on only one vitamin, but should also prescribe other associated vitamins.

6. Under all circumstances, after the emergency use of vitamins themselves, we should provide the needed vitamins by changes in the diet.

7. Night-blindness may be due to a lack of "A." (Effect upon the retina, a derivative of the ectoderm, neural.)

8. Xerophthalmia may be due to a lack of "A." (Conjunctiva, derivative of the ectoderm, surface.)

9. External ear: Dry scaly skin may be due to a lack of "A." (Derivative of the ectoderm, surface.)

10. Retrobulbar neuritis may be due to a lack of the B Complex, especially "B_1." (Derivative of the ectoderm, neural.)

11. "B_1" may be the therapy needed for herpes of the cornea. (Derivative of the ectoderm, neural.)

12. Peripheral neuritis, particularly as a complication of alcoholism, may be relieved by the B Complex — especially "B_1." (Nerves, derivatives of the ectoderm, neural.)

13. Transverse fissures at the angles of the mouth, a reddened denuded appearance of the lower lip, a magenta reddening of the tongue, and "cracked lips" may be relieved by "B_2." (Derivatives of the ectoderm, surface.)

14. Seborrheic plugs in the skin, eczema of the external ear, and "shark skin" over the bridge of the nose, may be quickly cured by "B_2." (Derivative of the ectoderm, surface.)

15. Keratitis and reddening of the conjunctiva may be due to a "B_2" deficiency. (Derivatives of the ectoderm, surface.)

16. Glossitis and stomatitis, with or without associated Vincent's infection, may be due to a lack of nicotinic acid. (Derivatives of the ectoderm, surface). Stomatitis is too frequently considered to be due entirely to a Vincent's infection, and we must have in mind that the underlying condition may be a lack of "B_2" or nicotinic acid.

17. Bleeding gums may be relieved by "C." (Blood-vessel walls and capillaries, derivatives of the mesoderm.)

18. In surgical cases with a low level of prothrombin, "K" is of value.

PROBABLE.

1. In a moderate "A" deficiency, it is probable that keratinization may be present in the mucosa of the nares and nasal sinuses, and most commonly in the trachea and bronchi. (Derivatives of the ectoderm and the entoderm.)

2. If we regard "fever blisters" on the lips and "canker sores" in the mouth as due to herpes, it is probable that "B_1" is of help. Nervous tissue, derivative of the ectoderm, neural.)

3. It is probable that a lack of "B_2" may be made evident, before general gross signs are present, by fissures at the angles of the mouth, and superficial vascularization of the cornea. (Derivatives of the ectoderm, surface)— with symptoms of photophobia and dimness of vision.

POSSIBLE.

1. It is possible that "A," and perhaps also "B_1" and "B_2," may so improve the condition of the mucosa of the nose, mouth and throat as to lessen the liability to infection. (Derivatives of the ectoderm and the entoderm.)

2. It is possible that hearing defects due to lesions of the cochlea may be improved by the B Complex, especially "B_1," "B_2" and nicotinic acid. (Cochlea, derivative of the ectoderm, neural.) Unfortunately, such restoration of nervous tissue does not often happen because of the type of chronic changes in the internal ear. Even granting that the lesion is due to a vitamin deficiency, we cannot expect a restoration of VIII Nerve function unless the sensory structures within the internal ear are viable. When due to a vitamin deficiency,

any sensory nerve degenerates beginning at its peripheral portion extending inward — up to its ganglion cells. If the ganglion cells have been destroyed, regeneration of this nerve cannot occur. The spiral ganglia of the cochlear nerve occur in groups in the internal ear itself. To them have come the dendritic fibers from the hair cells. From the spiral ganglia, these fibers continue to the nuclei in the medulla. Similarly the dendritic fibers from the vestibular end-organs proceed to Scarpa's ganglion and continue to the medulla. Therefore if we hope for an improvement in the function of the internal ear, whether cochlear or vestibular, it would seem necessary to postulate the following:

a. The impaired function must be directly due to a lack of vitamins; and

b. The cells of the spiral ganglia and Scarpa's ganglion must still be viable. If these ganglia are destroyed no regeneration is possible. If, however, the function of the hair-cells has been impaired by a vitamin deficiency and yet the cells of the spiral ganglia and Scarpa's ganglion are not destroyed, it seems reasonable to expect that regeneration can occur within the internal ear itself — just as regeneration has been proved to occur in peripheral nerve filaments in other parts of the body.

3. In cases of hyperesthesia of the VIII Nerve (Derivative of the ectoderm, neural), "B_1" may relieve tinnitus.

4. "B_1" may relieve alteration in the pitch and character, as well as the strength of the voice sounds — probably by relieving a neuritis of the laryngeal branches of the X Nerve. (Derivatives of the ectoderm, neural.)

5. "B_2" may prove of value in night-blindness when given in conjunction with "A." (Derivative of the ectoderm, neural.)

6. It is possible that mucous membrane ulcerations due to tuberculosis may respond to treatment with the B Complex. (Derivatives of the ectoderm and the entoderm.)

7. It is possible that "B_6" plays some part in the control of adolescent acne. (Derivative of the ectoderm, surface.)

8. It is possible that "C" may be indicated in some cases of epistaxis. (Blood vessels and capillaries of nasal mucosa, derivatives of the mesoderm.)

IMPROBABLE.

1. It is improbable that a lack of "B_2" produces cataract in the human as it does in rats; however. it may be wise to give therapeutic doses of "B_2" to human beings with incipient cataract. (Derivative of the ectoderm, surface.)

The observations given above are encouraging to the clinician. At last we are beginning to apply to the human the knowledge that previously had been limited to animal experiments. To be sure, for more than half a century cod-liver oil has been prescribed by wise physicians, long before vitamins were discovered; but now we know that the benefit resulted from the "A" and "D" in the oil.

For precise information, however, we must still depend largely upon the laboratory. Most of the experimental animal work has been for the purpose of discovering each individual vitamin and studying the effect of depriving an animal of each vitamin. It occurred to us to conduct experiments* that more nearly approach the clinical. No one food contains only one vitamin; and if a patient has a deficiency in one vitamin he also has a deficiency in other associated vitamins. Consequently in experiments on rats, brewers yeast was selected. It not only contains all the factors of the B Complex which have already been isolated, but probably also contains other factors of the B Complex concerning which definite information is not yet available. The immediate object of the first experiment was to deprive certain rats of the factors of the B Complex and to give the B Complex to the control rats. The details are presented in a previous editorial.[2] It soon became evident that the rats could not live over three weeks without the factors contained in the yeast. During the experiment certain of the deficient rats received the yeast — with marked improvement in two days. Certain of the con-

*These experiments were conducted under a grant from the Research Study Club of Los Angeles.

trol rats that had received the yeast from the beginning were then deprived of the yeast. In nine days these large rats had reduced in size; and the little deficient rats, continued on yeast, so increased in size that both groups weighed nearly the same. In this way one could easily make the big ones into little ones and the little ones into big ones, simply by withholding or giving the yeast.

The above experiment determined how much yeast would be required in order to keep the rats alive. It appears that a diet containing 4 per cent of yeast is necessary. The second experiment consisted in producing moderate and mild deficiencies in another set of rats, over a period of time — some of them for six months, which is a long time in the life of a rat, corresponding to many years in the life of a human being. From time to time one of the rats was sacrificed. It is most important in securing good specimens that the animals be perfused; otherwise artefacts are sure to appear, thus nullifying the experiment. The two objects of such a study were: *1.* to find out what would occur in the ear from a lack of the complete B Complex; and to compare such findings with those of W. P. Covell,[3,4] who for several years has made such elaborate studies of the effect of a deficiency in many individual vitamins; and *2.* to study the histologic findings in the nose, mouth, throat, larynx and trachea — both in the controls and in the deficient animals. This was of particular interest because to date it appears that no histologic studies have been made of the effect of any vitamin deficiency on the structures of the nose and throat.

A tentative report of the findings is made by Dr. Covell: In the sections so far studied, the mucosa of the turbinates, tongue, larynx and trachea showed very little difference from that found in the control rats. Such changes as were observed could not necessarily be ascribed to the yeast deficiency. In the ear, however, significant changes were found: Degeneration of the external sulcus cells; minor degenerative changes in the supporting cells and in the external hair cells of the organ of Corti; degeneration of the spiral ganglion cells, particularly in the middle and lower basal whorls of the cochlea, with total loss of some cells and various stages of degeneration in others; the cochlear nerve fibers between the organ of Corti and spiral ganglion showed fragmentation and

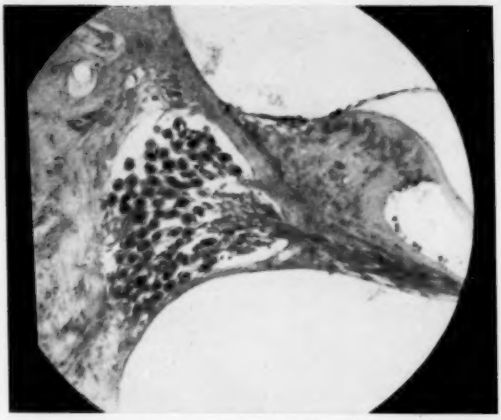

Fig. 1. The spiral ganglion cells in a mid-vertical section of the cochlea of a control rat which received yeast throughout the experiment. The cells are normal in appearance and show no changes whatever.

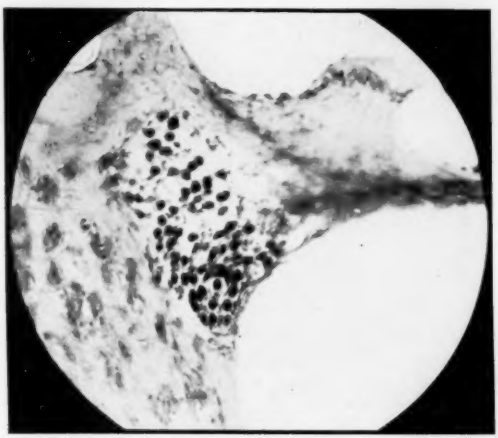

Fig. 2. The spiral ganglion cells in a mid-vertical section of the cochlea of a rat which did not receive yeast in its diet. The cells are shrunken, some are missing and all stain intensely with eosin.

reduction in the total number of fibers. A comparison of these findings with the previous studies on the ears of rats lacking a single vitamin of the B Complex in their diet, shows a similarity to deficiencies in vitamins B_1, B_2 and B_6 — each of which affected the same structures. In the previous stud-

ies, the lack of "B_1" in the diet of the rat produced more profound changes than the lack of the other vitamins.

Comment on the rat experiments: In rats, a marked deficiency in yeast produces a rapid loss of weight; if yeast is then given, the weight promptly increases and the rats improve in behavior and general appearance, including an approach to normal in their coats; rats cannot even live without the factors contained in yeast — those that are continuously deprived of the yeast promptly die; in order to produce a deficiency, and yet one moderate enough to keep the rats alive, a diet containing 4 per cent of yeast is necessary; histologic study of such moderately deficient rats shows very little effect on the mucosa of the nose, mouth, larynx and trachea, but significant changes in the cochlea.

In noting the absence of marked changes in the mucosa of the nose and throat, we should bear in mind that these rats were not deprived of one of the important factors of the B Complex — nicotinic acid. To be sure they received none of it in the diet itself; but the rat, like so many of the lower animals, actually manufactures its own nicotinic acid. In other words, these rats had a full complement of nicotinic acid — of which it is naturally impossible to deprive them.

In clinical practice we have been limited to three methods of approach: *1.* Diet; *2.* Laboratory Tests; and *3.* Therapeutic Tests. In these methods of diagnosis, there are marked limitations. A study of the diet is not only laborious but by no means convincing, and at best leaves us with a very vague concept. The laboratory tests are becoming more available but are still restricted to large medical centers. A therapeutic test is one of trial and error — yet it can be of definite help, especially when given by the needle.

In addition to these methods it would seem that the embryologic approach now enables us, by a study of the lesion in the eye, the ear, the nose and the throat, to prescribe a vitamin which is known to have a preponderant effect upon a tissue, originating from one of three germ layers. Such an approach is definitely clinical. If further animal experiments can show the actual effect on each germ layer of *depriving the mothers* of each of the vitamins, the facts would be definitely known. However, even at the present time, the reported clinical experience seems to confirm the concept.

REVIEW OF THE LITERATURE FOR 1941-1942.

DR. ISAAC H. JONES and DR. WALTER P. COVELL, Los Angeles.

A remarkable survey of the rôle of vitamins in living things, whether plants or animals, is given by Williams[5,6] in a lecture which he entitles the "Social Implications of Vitamins." Increasingly, popular thought classifies our social organization as a thing apart from nature — something to be dealt with as seems to us expedient. The evidence of evolution lies largely in studies of *Morphology* — particularly from the shapes of the skeletal remains of living creatures which have left their imprints in the rocks. These fossils may lie but a few inches or few feet apart, vertically, in successive strata of the rocks and yet show major contrasts in their forms — and only relatively minor similarities. The study of the *chemical* descent of man, especially in our new knowledge of the vitamins, corrects the illusory sense of a gross, rapid and radical alteration suggested by morphology. Vitamin chemistry brings an intimate vision — in that we find a community of inheritance in living things — even though all similarities of their outward forms have been erased. All living matter is composed predominately of carbon, which of all the elements possesses the singular property of uniting with itself. In inorganic nature the compounds of elements are like the word signs used by the Chinese — there have to be as many signs as there are words. By contrast, carbon atoms resemble letters of an alphabet which can be linked together to form thousands of words. There are about as many compounds of carbon as there are words in the English language and the formulae of even simple ones often contain more characters than a German jawbreaker. Each of us has about 5 grams of glucose in the blood stream. Turn where you will, you will find it also in other blood streams — and in the saps of plants. Vitamins are the bits, the working ends, of the keys which unlock the stores of vital energy from glucose and other foods. Indeed, to the best of our knowledge and belief, vitamins are the master keys which perform the same function within the cells of all living things alike. Animals came much later than plants and can claim no share in the inventions already present in the plants. We who have long

boasted as the lords of creation, find that we are mendicants in nature's breadline and heirs of the grass of the fields. The revelation provided by vitamin chemistry seems sufficient to convince the skeptic that while nature has *altered* much in proceeding from the lowly ameba to Einstein or Dorothy Lamour, she has *preserved* even more, through all the vicissitudes of evolutionary history. Until the beginning of this century there were no generally accepted standards of food requirements; each judged for himself by taste and by his sense of fullness under the belt. Rats fed on the poor class English diet failed miserably; on the sixtieth day of the experiment they began to kill and eat each other. By contrast, rats fed a simple mixture of whole wheat and whole milk grew and reproduced normally through many generations. Simplicity of food seems associated with vigor — and epicurean delights of the table with declining civilizations.

As to the prevalence of malnutrition, a careful survey by Jolliffe, McLester and Sherman[7] led them to conclude that dietary inadequacies and malnutrition of varying degrees are of frequent occurrence in the United States. The nutritional status of an appreciable part of our population can be distinctly improved. If optimal nutrition is sought, not mere adequacy, then widespread improvement is possible.

An excellent up-to-date summary, with special application to VIII Nerve and conduction deafness, is given by Selfridge.[8] To simplify this subject, he gives the principal food sources of each vitamin and the obvious signs and symptoms of deficiencies in human beings. "A" deficiency: Xerophthalmia, night-blindness, photophobia, difficulty in reading at night, momentary blurring while reading, metaplasias of the conjunctiva and cornea, keratinization in the eye, ear, nose and elsewhere in the body, abscesses in the ear, mucous membranes and elsewhere, keratinization of the skin, and myelin changes in the VIII Nerve and other nerves. B Complex. "B_1" deficiency: Anorexia, gastrointestinal hypotonicity — constipation or diarrhea — polyneuritis, bradycardia, vertigo, hyperactive nystagmus (in rotated rats) — and degeneration of the VIII Nerve, spinal cord and other nerves. The B Complex is necessary for the metabolism of carbohydrates. "B_2" deficiency: Itching and burning of conjunctiva, photophobia, ciliary congestion, keratitis. The lips are reddened and shiny; maceration and fissuring at the angles of the mouth; sebor-

rhea in the nasolabial folds and scalp; purplish red tongue. "Nicotinic acid" deficiency: Pellagra, with its loss of weight, fatigue and gastrointestinal disorders. The undersurface and sides of the tongue become fiery red. Symmetric disturbance of the skin, on the face and arms and elsewhere. "B_6" deficiency: Skin lesions — seborrheic and desquamative ulceration of the ears and about the mouth. Hyperchromic microcytic anemia has been produced in dogs. "C" deficiency: Bleeding from nose, petechial spots in various parts of body, swollen and bleeding gums. Experiments have shown changes in the middle ear mucosa. "D" deficiency: Rickets. Selfridge considers that deafness is related to all the factors involved in growth — endocrines, electrolytes, amino acids and vitamins. He particularly stresses that the time to begin the prevention of deafness is really six months before conception — each parent should be taught that a normal diet is necessary in order to beget a normal healthy child; that such a diet should be continued by the pregnant mother; and that the same careful supervision should be given to the diet of the child, through infancy, childhood and adolescence.

The Lancet[9] reviews studies made in Finland by Nylund. The Scandinavians are large consumers of dairy products and eat few vegetables — so they rely almost entirely on animal fats for their "A." Nylund examined a group of students in 1938 and another group in 1940. Between these two dates dairy products had been rationed. Of the 1938 group, 79 per cent showed normal dark adaptation, 9 per cent were night-blind and 12 per cent were borderline; in the 1940 group only 48 per cent had normal adaptation, 29 per cent were night-blind and 23 per cent borderline. He also compared the findings in pregnant and nursing women (in whom the "A" requirements are known to be high) with those in a similar series tested in 1938. Here again there was a falling off in dark adaptation: From normal adaptation in 95 per cent and night-blindness in 5 per cent, the standard had fallen to normal adaptation in 65 per cent and night-blindness in 25 per cent, with 10 per cent on the borderline; with an increase of "A" in the diet, night-blindness was not present; it was found that dark-adaptation was fully normal if a minimum of 2,000 I.U. of "A" was supplied daily. Other investigators have put the requirements higher — some consider 3,000 to 4,000 I.U. to be necessary. The most reliable estimate of the daily requirements of pregnant and lactating women is 5,000 to

6,000 I.U. To obtain the most prompt and complete recovery, some have recommended 100,000 to 300,000 I.U. daily, whereas others have obtained the same result with amounts as low as 10,000 I.U.

A correlation between the amount of "A" in the blood plasma and the adaptation of the retina to dim light is offered by Josephs, Baber and Conn.[10] The desire to obtain evidence of a deficiency before anatomic changes have developed has led to the increasing use of these two methods by which it is hoped to achieve this object: *1.* The determination of ability to adapt to dim light; and *2.* the measurement of the blue color obtained by the addition of antimony trichloride to a petroleum ether extract of blood serum. The importance of a knowledge of the level of "A" in the blood is obvious, but mere knowledge of the level of "A" is of no value unless we are able to learn its significance in relation *1.* to storage, and *2.* to adequate distribution. It is well established that the blood level bears no constant relation to the stores; the only conclusion we can reach is that a high blood level is inconsistent with a deficiency. In the presence of a low blood level the question of deficiency, whether of stores or of distribution, is uncertain. In contrast, there is a definite relation between a very much prolonged adaptation time, a poor diet and a low "A." The results demonstrate the importance of "A" deficiency in prolonging the adaptation time; but just as in the case of the blood level of "A," a moderate prolongation of the adaptation time has little significance; one cannot say that because marked prolongation is presumptive evidence of an "A" deficiency, that a moderate prolongation is evidence of a milder deficiency. There are evidently other factors not yet evaluated that interfere with dark adaptation. Myopia is one such factor. In the cases studied, the blood level of "A" has the same significance as the adaptation tests, in regard to its use in diagnosis — and the same limitations. In each procedure we can obtain evidence of a relatively severe deficiency — in the absence of anatomic evidence; but we cannot yet by these means diagnose a mild deficiency or state that in any given case the "A" in the diet is insufficient for our needs. We can, if it is grossly deficient.

In a study of the amount of "A" in the blood and of the visual threshold with the Hecht and Shlaer dark adaptometer, Yarbrough and Dann[11] concluded that a single measurement

of the visual threshold is not a reliable indicator of "A"; and that the level of "A" in the blood is the most promising method of detection by a single test.

In a series of children, Bodansky, Lewis and Haig[12,13] found that the plasma "A" concentration was considerably more sensitive than the dark adaptation in detecting a deficiency in "A"; however, occasionally one may observe a normal level of "A" in the blood and an abnormal dark adaptation. It seems reasonable, therefore, that a full investigation of the status of "A" requires the dark adaptation test as well as the determination of the "A" level in the blood.

The relationship between the amount of "A" in the blood and liver, and the general nutrition, is discussed by Horton, Murrill and Curtis.[14] It is naturally important to correlate, if possible, the "A" content of human blood with the state of nutrition of the whole body. In such studies, the normal range was estimated in a large number of healthy subjects. In some instances, human subjects were placed on "A"-deficient diets and the blood levels of "A" were studied over periods of two to six months; however, it was not possible to give diets entirely deficient in "A" or to continue the diets for a sufficient time to reach critically low "A" levels. Also, it was naturally impossible in human subjects to correlate the amount of "A" in the blood with the amount in the liver. Consequently the writers used rats as the experimental animal, to aid in the interpretation of their data obtained on the human being. Blood and liver "A" concentrations were determined in rats during the course of depletion and also while they received definite quantities of "A." Eighty-six rats, 28 days old, received a basic diet containing no "A." Some of the rats received a definite amount of "A" at the beginning of the experiment; some received none throughout the study. The others were depleted of "A" and then divided into two groups, each group receiving different amounts of "A." Animals were killed at intervals during the experiment and the "A" content of the liver and blood was determined. When no "A" was included in the diet, the concentration in the blood and liver declined in a parallel manner. As the result of these experiments the authors consider that a determination of the amount of "A" in the blood is an index of the "A" nutrition of the body.

A different conclusion is reached by Leong[15] in his study of the relation of "A" in the blood to the general nutrition. He considers that a low "A" level cannot be considered as a definite sign of depleted reserves. The rat was found to be unsuitable for such studies because its blood level of "A" is normally too low to permit a reliable estimation. The plan of his study was to rear young puppies of about six weeks of age on a diet with no "A" content. When about six months old, the puppies received an "A"-deficient diet which was supplemented with graded doses of "A." Their relative, though not absolute reserves of "A" were thus known. The levels of "A" in their blood were determined at regular intervals, to see if they were related to the "A" reserves. The results indicated that it was not possible to lay down a normal "A" value for dog's blood; however, it was concluded that there is no danger of avitaminosis A in dogs so long as there are even traces of "A" in the fasting blood.

Of 143 persons in a low income group — $52 to $95 a month — Kruse[16] found that 99 per cent showed xerosis conjunctivae. 45 per cent showed gross lesions; the lesions of the other 54 per cent were detected by the biomicroscope — which shows early changes. It is a rapid, convenient and objective method of detecting a very early deficiency in "A." It permits examination of the limbus and cornea for an early deficiency in "B_2" (from which avitaminosis is easily differentiated); and further provides a much needed means for determining the dietary requirements for both "A" and "B_2." One hundred thousand units of "A" were given daily to a part of the group; the conjunctival lesions in nine completely disappeared and in all the others the lesions markedly receded to the point of near disappearance (as judged in all instances by examination with the biomicroscope). In all cases it required months for this recovery — even with therapy of high potency. Those persons not receiving therapy showed no improvement. This study suggests that xerosis *precedes* night-blindness as an early sign of a lack of "A." This work and the work of others suggest that in the population at large there is a marked prevalence of avitaminosis A.

Berliner,[17] however, considers that most of the gross as well as biomicroscopic findings which Kruse[18] reported are really due to presenile and senile alterations of the conjunc-

tiva. After careful study he considers that these "spots" on the conjunctiva are *pingueculae* — which are in the connective tissue, do not involve the epithelium and are commonly encountered in the general population in individuals over 40 years of age.

The relation of "A" deficiency to lesions of the nervous system has long been in a state of confusion. Wolbach and Bessey[19] suggest a solution to this problem; an "A" deficiency, when started at an early age, causes a disproportion in growth between the central nervous system and its osseous envelopment. Experiments were made on white rats, guinea pigs and dogs. The writers observed that paralysis and nerve lesions invariably occur if the deficiency is established before the eighth week of life. Their experiments indicate that, when there is an "A" deficiency, the nervous system continues to grow at a normal rate. The rats retained on an "A"-deficient diet invariably became paralyzed and when dissected showed the characteristic relative overgrowth of the nervous system. The litter mates which received "A," with restriction of the quantity of food, did not show signs of nerve lesions; and on dissection, the relations of the nervous system to the bone were within normal limits. The deduction is made that the central nervous system grows at a rate approximately normal for the species, whereas the growth of bone is promptly retarded. In brief, they found that there is no evidence that an adequate amount of "A" or a deficiency of "A" has any effect on the nervous system. The writers conclude that the nervous lesions of an "A" deficiency are wholly of mechanical origin. There appears to be a normal growth of the central nervous system and an impaired development of the bone which surrounds it.

Spiesman[20] reports the results from massive doses of "A" and "D" in the prevention of the common cold. Fifty-four patients were studied; all had a record of frequent colds — five to seven colds each winter for seven years previous to the study. All were free from pathologic conditions, particularly of the respiratory tract and sinuses. Neither "A" nor "D" in massive doses produced immunity to the common cold, when given separately; but when "A" and "D" were given together, 80 per cent showed a significant reduction in both the number and severity of common colds.

Mills[21] describes a warm-blooded animal as an energy conversion machine — not an efficient one, however, as only 20 to 30 per cent of energy is used. The efficiency is about the same as a good gasoline motor, but far below the 37 per cent from the Diesel engine. The human body is, therefore, compelled to dissipate 70 to 80 per cent as waste heat. If this is not well accomplished, there occurs a slowing down of cellular combustion and a more sluggish pace of life — slower growth, retarded development, reduced fertility, lessened resistance to infection, and lowered energy for thought and action. Human growth is retarded in the tropics, whereas in the temperate zones it proceeds lustily. If cellular combustion is slowed down by external heat, the vitamin requirement for handling the food rises sharply; twice as much "B_1" is needed at 90° F. as at 65°. Not only are the B Complex requirements greater in the moist heat of the tropics, but the food in the tropics contains less of the B Complex. It takes five years in the tropics to produce a 1,000-pound steer; in temperate zones, one and one-half to two years. A 200-pound hog is produced in Panama in 12 to 15 months; in Northern United States in six to seven months. "B_1" in too large doses may be toxic. The author has noted toxic symptoms — insomnia, irritability, headache, rapid pulse, tremor, weakness, collapse (in one instance, syncope and near approach to death) from taking "B_1." In all instances, prompt recovery followed the discontinuance of the "B_1." We should have better control of "B_1" dosage by excretion studies.

From the point of view of preventive medicine, Sebrell[22] regards as conclusive the evidence that there is a great opportunity to improve the health of the nation by increasing the B Complex content of the diets of a considerable part of our population. He regards the B Complex deficiency as the greatest medical problem in the field of nutrition. Of the eight known factors of the B Complex, four appear to be needed by man — "B_1," "B_2," nicotinic acid and pyridoxine. Deficiencies in the other factors of the B Complex have been shown to cause symptoms but, to date, only in experimental animals.

The work of Sherman and Pearson[23] is commented on in a recent editorial in the *Journal* of the American Medical Association.[24] The average American consumes each day about $6\frac{1}{2}$ ounces of white flour — and this amount provides about

one-fourth of the average *caloric* requirement. Bread today is not the same as the ordinary white bread of previous years. Bakers now use greater quantities of dried skim milk which has almost the same "B_2" content as whole wheat bread made with water. There are three methods for making enriched bread: Using enriched flour; incorporating a concentrate of either milling products of wheat or an artificial preparation of the desired composition; and the using of yeast which has enhanced nutritive value. A slice of the old white bread has about 0.02 mg. of "B_1"; enriched bread about 0.07 mg.; and whole wheat bread about 0.1 mg. Of nicotinic acid, the amounts are 0.2, 0.4 and 0.7 mg. — the enriched white bread again being intermediate in value between that of white bread and that of whole wheat bread. The iron content is 0.1, 0.3 and 0.8 mg., respectively, for a slice of white, enriched or whole wheat bread.

In reviewing the status of the known factors of the B Complex, Sebrell[25] notes that the following have been chemically identified: "B_1," "B_2," nicotinic acid, "B_6," pantothenic acid, choline and inositol. Another known member is biotin but its chemical structure has not been clarified. In human medicine "B_1," "B_2" and nicotinic acid are of the greatest importance. "B_6" is still questioned in regard to clinical use. Similarly, the importance of pantothenic acid, choline and inositol has been shown only in animals; however, it would be remarkable if substances of such importance to an experimental animal should not also be of some importance to man. Dietary surveys indicate that at least one-third of the American population has an inadequate diet. A move in the right direction is that of enriching the white flour with "B_1," nicotinic acid and iron and in some instances with "D" and calcium. When supplies become available, "B_2" will be added. It would be best if we used the lightly milled flour; but the American public does not like the color or the taste — so the next best thing is to conceal the material in a tasteless and colorless form which enables them to have their "angel-food cake" and still get the vitamins.

Careful studies were made by Keys and Henschel[26] to determine whether our army rations are adequate. Two hundred and fifty-six experiments were carried out on 26 soldiers who were studied before and after standardized exercise on a motor-driven treadmill. Certain soldiers received large extra

doses of "B_1," "B_2," nicotinic acid, "B_6," pantothenic acid and "C." These vitamins were given over periods of four to six weeks, alternating with equal periods in which the soldiers received placebos. In these young men there were no indications of any effect on muscular ability, endurance, resistance to fatigue or recovery from exertion. The present army rations, therefore, appear to be adequate. Healthy young men expending an average of 3,700 to 4,200 calories daily do not need a daily supply of more than 1.7 mg. of "B_1"; 2.4 mg. of "B_2"; and 70 mg. of "C."

Abels, Rekers, Martin and Rhoads[27] made an elaborate study of atrophy of the tongue and oral leucoplakia. Both of these conditions are especially important because they are of a very possible precancerous nature. Cancer is frequently seen in association with leucoplakia and has been observed to develop in it. In a large series of patients, they found that the giving of brewers yeast was followed occasionally by a complete or partial remission of the papillary atrophy of the tongue and oral leucoplakia. Their observations suggest that there is a relationship between the appearance of such lesions and a lack of certain dietary factors present in yeast.

In their first reports, Williams and Mason[28,29,30] described the effects of a "B_1" deficiency on eight individuals. The maximal intake of "B_1" was 50 units — appreciably less than the 300 units required by the League of Nations Health Committee. The first symptoms minutely resembled a condition which any discriminating phychiatrist calls neurasthenia. At the end of the period of deprivation the clinical picture was that of anorexia nervosa. The authors concluded that when a diagnosis of neurasthenia has appropriately been made, we should look for a "B_1" deficiency. Recognizing that such a severe restriction of "B_1" is not often encountered in clinical practice, they undertook a new experiment in which they restricted 11 women to only 133 to 150 units daily. These women were under close observation, continuing in various activities in the hospital. Large stores of foods together with standardized techniques of cooking made it possible to prepare a uniform diet, in which the content of "B_1" varied by only a few micrograms throughout the period of study. Urinalysis was made once a week. Disturbing symptoms developed in one woman after 93 days; three continued on the diet for 132 days; five for 169 days; and two for 196 days. In

general, the more active subjects were the first to show symptoms. All showed faint heart sounds and low blood pressures; when standing, eight had dizziness and pallor; during rest the pulse rate was slow but on moderate exertion it exceeded normal limits. Five subjects showed a considerable degree of anemia — which was not relieved by giving iron, copper, protein and various vitamins. After several weeks all became depressed, irritable, quarrelsome, fearful, inefficient in their work, inattentive to details of their tasks, uncertain of memory and lacking in manual dexterity. These psychic disturbances disappeared when "B_1" was added to the diet — without the knowledge of the subjects. The writers consider that a physically normal woman can survive for six months on a daily intake of 0.2 mg. of "B_1" per 1,000 calories of a mixed diet, but the health is improved when 0.5 mg. is provided. The data indicate that the optimal intake of man is not less than 0.5 mg. and not more than 1 mg.

The importance of "B_1" in nutrition is emphasized by the experiments of Hauschildt[31] on albino mice. At the time of weaning, 5 mg. per day maintained body weight and 10 mg. proved to be the minimal level for normal growth. Less than 5 mg. per day resulted in loss of weight and eventual death.

"B_1" deficiency in birds is presented by Swank and Bessey.[32] The food intake and the amount of "B_1" were varied, to produce a starvation and deficiency of varying severity. The pigeons that receive a highly purified diet, with no "B_1," in quantities sufficient to prevent large weight loss, invariably developed opisthotonus. When the ration was made only partially adequate by the addition of "B_1," ataxia and leg weakness developed in all pigeons — and a cardiac failure in many. The intramuscular injection of "B_1" promptly relieved the opisthotonus and the mild cardiac failure.

Wooley and Sebrell[33] consider that there is much evidence suggesting a relationship between deficient diet and infection in experimental animals. Their own work with mice confirmed this concept. They inoculated mice with Pneumococcus Type I and noted that the mice deficient in "B_1" and "B_2" were more susceptible to a fatal infection than the mice fed on a diet containing enough of the vitamins for good growth.

Riboflavin deficiency in the dog is reported by Street, Cowgill and Zimmerman.[34] The dogs were classified into three

groups: Those that received only the basic diet; those that received a diet that contained enough riboflavin to support life but not enough to maintain health; and those that received the same amount of diet but also received riboflavin daily — 25 mg. per kilogram of body weight. In brief, the only difference in the three groups was the amount of riboflavin given as a supplement to the basic diet. The dogs that received only the basic diet collapsed, usually in from 100 to 500 days. Animals will recover from this collapse only if they receive riboflavin before the attack has progressed too far. There was a loss of weight from 30 to 41 per cent. In the chronic deficiency group, the weight dropped more slowly. Observations were made of the abilities of the dogs to perform on an obstacle board, a turntable, and in balancing themselves on their hind legs. Histologically, the essential lesion is a demyelination of the peripheral nerves and of the posterior columns of the spinal cord. In the chronic deficiency dogs, gliosis replaced the injured posterior columns. It seemed justifiable to conclude that the peripheral lesions preceded the lesions in the cord. This demyelination process extends centrally along the posterior nerve roots; the degree of demyelination becomes greater on prolonging the period during which the deficient diet is given. The neurologic symptoms of riboflavin deficiency in dogs are very different from those in "B_1" deficiency — in which one of the first noticeable effects is a spasticity, causing a striking abnormality in gait. In contrast to this, dogs on a diet low in riboflavin continue to exhibit a normal or nearly normal gait, even when degeneration of the nervous system has progressed to the point where the deep reflexes are lost.

A study of 28 cases of corneal disease treated with "B_2" was reported by Cosgrove and Day[35] — with varying results. Allergic cases showed no improvement. In cases of corneal disease in which no definite etiologic factors could be determined, some responded miraculously. In one case there was a recurrence of the keratitis when the "B_2" was omitted from the diet. The cases of interstitial keratitis associated with hereditary syphilis responded more rapidly with the administration of "B_2" than when antisyphilitic treatment alone was given.

A comment on the treatment of Vincent's angina with nicotinic acid is given by Rosenblum and Jolliffe.[36] It is impor-

tant to differentiate between the true Vincent's angina and the mere presence of fusiform bacilli and spirochetes that may be found in patients with a nicotinic acid deficiency. True Vincent's angina does not usually respond to treatment with nicotinic acid; but a cure can result in those in which a deficiency of nicotinic acid has provided the environment necessary for the proliferation of the Vincent's organisms.

Ashworth and Sutton[37] have reported evidence indicating an inter-relationship between hormones of the anterior pituitary and the utilization of the B Complex. In a number of instances pellagra, refractive to vitamin therapy, was cured or improved by giving the extract of anterior pituitary. They had previously noted the tendency to exacerbation of the symptoms of pellagra during the menstrual cycle. One of the early symptoms observed in all these patients was a tender and painful nasal mucosa. In a series of cases they made observations on the effects of estrogens on patients classified as having subclinical pellagra. In all cases frank evidence of B Complex deficiency appeared; polyneuritis ("B_1" deficiency), cheilosis ("B_2" deficiency) and glossitis, cutaneous lesions and psychosis (nicotinic acid deficiency). The estrogens appear either to increase the demand for the B Complex, or to suppress its utilization. The appearance of tenderness and pain in the nasal mucosa appears to be a symptom of the full physiologic effect of estrogen, particularly in persons with a B Complex deficiency.

In evaluating vitamins in skin diseases Novy[38] considers that cutaneous reactions are common from therapeutic doses of the B Complex and considers that we should be on our guard when giving these vitamins. He also observes that increased pigmentation of the skin occurs when there is a low "C" content in the blood.

As yet we do not know any signs or symptoms that are characteristic of a pantothenic acid deficiency in the human; however, it would seem that if any substance is excreted in an appreciable amount it must play a definite part in human nutrition. Wright and Wright[39] made quantitative studies of pantothenic acid excretion. In 29 normal individuals the mean daily excretion was 3.42 mg. — which must have a significance.

Hjorth[40] has studied the influence of "C" on carbohydrate metabolism. He determined the glucose tolerance curve in patients that had a low "C" content of the blood serum, and found that they assimilated carbohydrates less rapidly than those with an ample supply of "C."

In a rural North Carolina community, tests by Milam and Wilkins[41] showed very low levels of "C" in the plasma. It was found that these individuals had had a very low intake of foods that are rich in "C." Thirty-four children then received an adequate diet, although of low cost, over a period of six weeks. At the end of this short period, there were striking gains in the "C" plasma levels.

After reviewing the chemical methods of determining a "C" deficiency, Trier and Pedersen[42] conclude that the border between normal and pathologic values of "C" concentration in the blood is still uncertain; also that the laboratory diagnosis of a "C" deficiency may not be accompanied by typical clinical symptoms.

Encouraged by the reports of others, Harvey and Hume[43] studied the effects of giving synthetic "E" in patients with progressive muscular atrophy, amyotrophic lateral sclerosis, progressive muscular dystrophy, amyotonia congenita, myotonia dystrophica, multiple sclerosis and dermatomyositis. Their own studies of the nervous systems of suckling rats from "E"-deficient mothers gave them the hope that "E" might be of value in certain human nervous diseases. Ninety patients were treated; the report, however, is limited to 60 patients because the others received less than 40 days' treatment. All patients received a diet rich in "E," which in many instances was supplemented with wheat germ oil or Wesson oil. Many had previously been treated vigorously with the B Complex. Synthetic "E" was given to one-half, in the form of alphatocopherol and the other half received alphatocopherol acetate. The alphatocopherol was at first given intramuscularly; later this was abandoned for lack of evidence in its favor and the treatment was continued by mouth. Of 16 patients with amyotrophic lateral sclerosis the disease appeared to be arrested in four. Only two of the 18 patients with multiple sclerosis showed remissions lasting six and 12 months respectively; but since such remissions are common in this disease, it would be a fallacy to assume that they were

due to the treatment by "E." The authors consider that the results during 14 months' experience with alphatocopherol treatment of these nervous diseases does not warrant an optimistic view; and they conclude that the most one can expect from "E" therapy is retardation of the disease process.

After giving a review of available information about "K," Hult[44] notes that it is only when prothrombin has been reduced to about 20 per cent of the normal that there is a tendency to bleeding. Blood transfusion has for a long time been utilized as a hemostatic agent in surgical cases associated with jaundice. The temporary improvement in the blood coagulation is now considered as due to the prothrombin supplied by the transfusion.

Laboratory and clinical studies on the intravenous use of synthetic "K_1" are given by Seligman, Hurwitz, Frank and Davis.[45] Various substances with "K" activities have served to relieve the bleeding tendency associated with prothrombin deficiency — in obstructive jaundice, hemorrhagic disease of the newborn, various disorders of the liver, and of the intestinal and biliary tracts. The lack of solubility in water of naturally occurring "K" is responsible both for the development of a large proportion of clinical "K" deficiency — and also for much of the difficulty in therapy. The earliest effort at "K" therapy made use of crude extracts of varying potency. The isolated principles were used as soon as they became available. Because of their insolubility in water, therapy was largely confined to oral administration, with the addition of bile salts when these were absent from the intestine. The need for an effective parenteral method of therapy became apparent. Nausea, vomiting, intestinal obstruction or other types of interference with intestinal absorption frequently prevented restoration of normal blood coagulability — often in the very patients most in need of effective treatment. Both the subcutaneous and intramuscular injections proved to have too slow an effect, and a method was devised of preparing "K_1" in colloidal suspension for intravenous administration. Such therapy has been found to be rapidly effective, the uncertainties of intestinal absorption are eliminated, and the action of the drug has been prolonged. The blood prothrombin level is very rapidly restored; this may occur even in a moribund patient. The prolonged effect of large doses sug-

gests the possibility of storage of "K_1" within the body. The intravenous route also avoids the changes in chemical form which may occur within the intestinal tract.

The intravenous use of "K" in 54 surgical cases is reported by Olwin.[46] The intravenous route is indicated in patients who have nausea and vomiting, and those with obstructive jaundice that require the bile or related material to be given with the "K" (and these often contribute to nausea already present); in patients in which the "K" is poorly absorbed from the gastrointestinal tract; and in those cases in which the response of a damaged liver to "K" is to be used as a measure of hepatic function — thus requiring a control of the exact amount of the "K" that gets into the blood stream. As to the question of intravascular clotting from an overdose of "K," from this study there appears to be a limit to the level to which prothrombin can be elevated. In none of the cases was there any evidence of thrombus formation. Several synthetic compounds were administered intravenously to patients with lowered prothrombin levels; the result was an elevation of the prothrombin. No toxic effects were observed.

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IN MEMORIAM

CURTIS CLYDE EVES, M.D.,

1875-1942.

Dr. Curtis Clyde Eves, prominent ear, nose and throat specialist, died at Pennsylvania Hospital, Philadelphia, Sept. 22, at the age of 67 years. Dr. Eves was born at Millville, attended the University of Vermont, and graduated from the old Medico-Chirurgical College of Philadelphia in 1905. He served his interneship at New York Eye and Ear Infirmary, doing post-graduate work in Vienna. From 1912 until 1920, Dr. Eves was on the staff of Episcopal Hospital and he was also a former head of the ear, nose and throat service at Bryn Mawr and Pennsylvania Hospitals, where until the time of his death he was consultant.

He was a Fellow of the College of Physicians and chairman of its section on otolaryngology; a Fellow of the American Laryngological Association, the American Otological Society, and of the American Laryngological, Rhinological and Otological Society.

He is survived by his widow, Mrs. Glodean Smith Eves.

T. E. W.

BOOK REVIEW.

Textbook of the Ear, Nose and Throat. By Francis L. Lederer, B.Sc., M.D., F.A.C.S., Professor and Head of Department of Laryngology, Rhinology and Otology, University of Illinois College of Medicine, Chicago; Chief of the Otolaryngological Service, Research and Educational Hospital; and Abraham R. Hollender, M.D., F.A.C.S., Assistant Professor of Laryngology, Rhinology and Otology, University of Illinois College of Medicine, Chicago. Five hundred ninety-five pages with Index and 170 illustrations. Philadelphia: F. A. Davis Co., 1942.

This book has an impressive cover, is printed on good paper and is profusely illustrated.

The authors state in the preface that, in view of the limited time spent in otolaryngology in the medical school curriculum, they are endeavoring to present a suitable textbook to supplement lectures and quizzes. They state that compends do not satisfy the high standard of modern medical teaching.

A textbook to supplement lectures should present all side of controversial subjects together with an adequate bibliography. The student is thus stimulated to think for himself and not to accept woodenly the "facts" on a printed page.

The book that the authors present as a "suitable textbook" has all the characteristics of a compend without its essential brevity. It contains no bibliography; controversial subjects are presented as facts with no mention of differing opinions. The various tables tend to complicate rather than to clarify the subjects under consideration.

In this reviewer's opinion the book fails as a textbook of ear, nose and throat and has no place in any medical school library.

T. E. W.